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Original Communications

CARDIAC INFARCTION (CORONARY THROMBOSIS); AN EASILY DIAGNOSABLE CONDITION*

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BOSTON, MASS.

WHEN I ended my medical school course, now just twenty-five years ago, cardiac infarct, the result of coronary thrombosis, had been shown to me in the postmortem room, but I can recall no reference to cardiac infarction or, as it is sometimes termed, coronary thrombosis, as a condition to be recognized during life. My teachers of that day seemed unable to make that diagnosis in the clinic. Today I find that the fourth-year medical students in my wards at the Peter Bent Brigham Hospital consider it in rendering a diagnosis on patients assigned to them for history and physical examination, and adopt or eliminate it with a very considerable degree of accuracy. In other words, the students of today diagnose with much accuracy a condition that was hardly known to the medical students of twenty-five years ago.

What has caused this change? It has come in the main as the result of the careful clinical study of patients by observers willing to take the time to record a thorough history and physical examination and then thoughtfully to consider this data in relation to the anatomical conditions found at the postmortem examination. No special, intricate, new methods of observation have played any essential part in the recognition of this clinical entity, though the electrocardiogram in some patients yields data helpful in making the diagnosis.

It seems to me worth while to keep this in mind in a day and time when chemical methods tend to overshadow the importance of pathological studies and considerations of function may turn thought away from those of structure. Notwithstanding the developments in chemistry and physiology, pathological anatomy has lost none of its impor-

*Presented September 18, 1925, at Seattle, Wash., before the Washington State Medical Association.

tance in the training of medical students and the progressive education of practicing physicians. The habit of careful clinical study of your patients with a checking up of clinical data by postmortem examination remains the greatest school of postgraduate medical study, and it is most unfortunate that we, as physicians, have allowed ourselves to fail to get the help that would come from frequent postmortem examinations on the patients that we have studied during life.

To my mind it is highly discreditable to American medicine that we tolerate so low a percentage of postmortem examinations in our hospitals and have almost entirely given them up in private practice, thereby losing a most valuable opportunity to advance our knowledge of medicine. We have found at the Peter Bent Brigham Hospital that effort on the part of the staff will yield an autopsy percentage increasing in ratio to the intelligence of the clientele, which means that it is easier to secure permission for autopsies on private patients than on public ward ones. Patients with imperfect knowledge of English, from lack of understanding, swell the number of refusals, while Jewish patients make the largest percentage of those who decline to permit autopsies; basing their refusal on a claim of forbidding religious tenets, a claim that the better educated rabbis do not support. Jewish physicians, to my mind, have been particularly remiss in not urging autopsies on their clientele, correcting this claim of a forbidding tenet in the Jewish belief. An active propaganda by them in favor of postmortem examinations would do much to increase the frequency of autopsies especially in certain sections of this country. However, by no means all blame should be placed on the Jewish physicians, for those of other religious persuasions are culpably negligent in seeking autopsy permits on their patients. All of this is somewhat of a digression from my main topic; precipitated, however, by the importance that pathological-anatomical study has been in developing our ability to diagnose cardiac infarction as a clinical entity.

Though, as already pointed out, in my own student days, little was heard of cardiac infarction as a clinical syndrome, yet to my old teacher, William Osler, should be given much of the credit for the correlation of the clinical and pathological findings in this condition; his publication coming some ten years after my graduation. Sir Clifford Allbutt, too, recognized and described the condition. George Dock and James B. Herrick of our present group of clinicians added much to our knowledge of the clinical aspects of cardiac infarction, especially the recognition of the form that recovers from the attack, for it is by no means a fatal disease. The clinical studies of these men have been rounded out by the experimental work on animals and the electrocardiographic studies on both animals and man made by F. M. Smith and others. Today, as I am here emphasizing, as a result of the observations of these men, cardiac infarction stands out as a clean-

cut clinical entity, easy of recognition by any practicing physician who knows the symptoms and usual findings. Simple bedside methods of examination suffice to make the diagnosis in most cases, so there is no reason why each and every one of you should not diagnose it correctly in your own patients.

Why, you may ask, is it important correctly to diagnose this condition? In the first place not at all infrequently the unrecognized case is submitted to a laparotomy in the belief that the pain in these patients, which may be referred to the abdomen, originates there from some lesion of the abdominal organs capable of cure by surgery. Symptoms are fulminating and alarming; emergency measures are inaugurated by the surgeon without thoughtful consideration of symptoms and careful study of the patient; the issue is a fatality. Too often there is no autopsy or only an examination of the abdomen through the operation wound. The surgeon learns nothing from his experience; his mistake remains unrecognized; with a similar situation in another patient he probably repeats his procedure with like result.

In the second place, a differentiation from angina pectoris is not made. Perhaps cervical sympathectomy is advised. Of course in cardiac infarction it does no good and may precipitate a fatal outcome. The reports of cervical sympathectomy for angina pectoris already contain some cases, unsuccessful ones as far as surgical therapy is concerned, which would seem to have been those of patients with cardiac infarction. Cervical sympathectomy is contraindicated in cardiac infarction and so cardiac infarction must be recognized in the satisfactory selection of patients suitable for cervical sympathectomy.

In the third place diagnosis of the condition is important in treatment. The chances of having a functionally efficient heart following a recoverable infarct of the heart muscle depends in very large measure on how the patient is treated immediately after the lesion develops, and, perhaps of greater importance, how the régime of convalescence is planned. Recognizing what has happened to the heart muscle is the most significant step in planning the treatment.

What are the significant findings in cardiac infarction? First as to history, many patients give a story of preceding precordial distress ranging from very slight transitory discomfort, extremely often interpreted by the patient and physician as indigestion, to definite attacks of angina. The various forms of preceding distress have in common abrupt onset, short duration, usual association with exertion, emotion or digestive activity, and location beneath the upper end of the sternum with or without radiation to the arm, ordinarily to the left arm. In another smaller group the discomfort, otherwise the same, is localized in the epigastrium. A very considerable group of patients have experienced no preceding distress. With extremely rare

exceptions the patient is past forty years, with the curve of incidence rising sharply to its maximum in the decade between fifty and sixty and then gradually falling. The youngest in our series was thirty-one, but this was a clinical diagnosis in a patient who recovered and so subject to error of diagnosis. The youngest patient with autopsy confirmation was forty-two. By decades patients with the diagnosis of cardiac infarction range in our series as follows:

30-39	years	of	age	5	cases
40-49	"	"	"	11	"
50-59	"	"	"	16	"
60-69	"	"	"	28	"
70-79*	"	"	"	11	"

More often than otherwise the patients have had no or very slight evidences of cardiac insufficiency. Very few have evidences of valvular lesion.

Most important in the history is the description of the symptoms associated with the occurrence of the infarction. There are two groups of patients, a large group in which pain predominates over all other symptoms and a small group without pain, having collapse, a sense of impending dissolution, and usually dyspnea as the chief symptoms.

The group with pain is more easily diagnosed because the pain is of such a severe, persisting type, and is at once recognized by the patient as something entirely different from any pain of his past experience, even though he has had typical attacks of anginal pain. This pain most often is located behind the sternum, especially behind its upper portion. At times it is entirely below the diaphragm in location. It is almost always a deep-seated pain. Frequently it radiates, most often down the left arm, next along the left side of the neck. It persists; its duration varies, but as a rule it is measured by hours, though it may fluctuate in intensity. The patient speedily recognizes that nothing that he can do relieves the pain; hence there is no characteristic attitude or position assumed by the patient. In some swallowing, in others any exertion, aggravates the pain, but at times eating or moving about seems in no wise to influence the pain. To see the patient during an attack removes all doubt as to the genuineness of the pain complained of. The face shows distress, anguish, apprehension; the skin is bathed in cold sweat; the color is usually pale, or ashen gray, while cyanosis is uncommon. Occasionally the skin shows a red flushing. It is obvious that the patient is suffering greatly and that his condition is serious.

Patients describe their pain variously. It is worth while quoting some of the descriptions from our records as given by our patients:

*The oldest in our series was actually seventy-six; of this age there were two patients.

"Agonizing substernal pain which lasted for forty-eight hours, alternating in intensity from real agony, of which the patient says he did not care whether he lived or died, to a dull aching pain. With each inspiration the intensity of the pain was tremendously increased, so much so the patient contented himself with rapid, shallow breathing. There was no radiation of the pain."

"Severe pain awakened the patient at 4 A. M. This pain was in the left elbow, spread to the hand and shoulder, then over the precordium and then through to between the scapulae behind. The pain was steady, sharp, and did not move from place to place, but occurred in all places named at the same time. She suffered much and had to sit up and fight for her breath."

"While sitting in a chair at the table the patient was suddenly seized with severe, excruciating pain along the lower left costal border at the anterior axillary line. The pain was very severe; the patient thought that he was going to die. He had a choking sensation and much difficulty in getting his breath. The patient said he felt as though someone was sitting on his chest. The spot was tender and continued to ache for about three hours."

"When on a train, while quietly reading a paper after an ordinary day of no unusual excitement, the patient was suddenly seized with a terrific pain, sharp and knife-like, over the heart. Later it became a gripping ache, spreading over the whole chest, radiating to the left shoulder and down the left arm to the fingers and down the right arm to the elbow. It continued unabated for five hours and it was so severe that the patient thought he was going to die and really wanted to die."

"While standing in front of the fire station one evening the patient, a fireman, was suddenly seized with a terrible pain across the front of the chest and in both shoulders, in front and in back. The pain was described by the patient as follows: 'It was like you were in a vise and someone was squeezing it. It was so severe as to bring tears to the eyes.' He had a choking sensation with acute shortness of breath, his breath coming in gasps."

"At noontime the patient was suddenly taken with a terrific attack of pain that gripped his chest and he broke out into cold perspiration and became prostrated."

"After an unusual amount of exertion the patient had a sudden attack of stifling pain in his chest, at which time it was very difficult for him to breathe. The pain was so severe that he had to lie down on the floor in his office. He sweated profusely and had marked dyspnea."

Gastric symptoms are very commonly seen, such as loss of appetite, nausea, vomiting. Patients frequently describe their condition as resembling some previous attack of indigestion, though every feature is very much more intense than ever noted before. If one goes carefully into the past history of patients, one so frequently gets a history of what the patient calls infrequent attacks of indigestion without any recognized precipitating cause, that one is led to think that these so-called indigestion attacks are really occasioned by slighter vascular disturbances in the myocardium. The phases of the symptomatology of cardiac infarction regarded by the patient as evidences of indigestion perhaps explain why our daily newspapers with great frequency attribute the death of notables to "acute indigestion," a condition which, as a cause of death, is in all probability actually limited to a very few examples of poisoning, including possibly a rare case of food poisoning. I feel very sure that a postmortem examination of

many of these notables would reveal a cardiac infarct. Certainly most of them fall in the age group of most frequent incidence of cardiac infarct and strange indeed would it be for actual acute fatal indigestion to spare those under forty years of age, while being frequent in those over forty, as it most certainly does in our newspaper reports. I often wonder whether the physicians of the country really make the diagnosis "fatal acute indigestion," or whether it is considered a blot on the family tree to die of cardiac infarction or apoplexy or other probable cause of death in these cases of "acute indigestion." After all, isn't the connotation of death from acute indigestion with its implication of gluttony, riotous living, etc., a worse stigma? I hardly think the diagnosis originates very often with the physician in charge.

Dyspnea is a prominent symptom in nearly every patient with cardiac infarction. A striking characteristic of it is the disproportion so often noted between the degree of dyspnea and demonstrable lesions of heart and lungs. I have seen a patient, who, while lying perfectly quiet in bed, would show but a very slight increase in respiratory rate and yet the effort of changing position in the bed would cause her to gasp for breath. This patient showed but trivial physical signs of cardiac or pulmonary lesion. She was one of our patients who had had practically no pain and the diagnosis of cardiac infarction, correct as confirmed at autopsy, was based on this disproportion between dyspnea and physical signs of cardiorespiratory lesion.

A number of the patients show a dyspnea characterized by rapid, deep breathing, in a way suggestive of the air hunger of acidosis, but in rate more rapid and so like the dyspnea often seen in pulmonary embolism. Though dyspneic, few patients are orthopneic and, as already mentioned, cyanosis is not prominent and may be entirely absent. In these respects they appear strikingly different from patients with the usual forms of cardiac insufficiency.

Of physical signs perhaps the more constant and important one is evidence of a weak cardiac action with a poor pulse showing, not infrequently, arrythmia. The heart usually is moderately enlarged but this scarcely helps in diagnosis. Murmurs are of no significance; systolic apex murmurs are often heard. Pericardial friction sound, unfortunately rarely present, when it does occur is of great aid in diagnosis along with the other features. Peripheral arteries of course show some evidences of sclerosis but often it is scarcely disproportionate to the age of the patient. Most surprising it is at times to find almost no signs of arteriosclerosis. Blood pressure is practically always lowered for some time after the attack and this is a helpful sign in diagnosis and its rise toward normal is of good prognostic omen.

Crackling râles at the bases of the lungs are nearly always present and usually persist except in recovering cases, and in these they may be heard for a long time. Often they are numerous and widely scat-

tered in the lungs, causing the picture of acute pulmonary edema. These râles, along with evidences of weak heart action, are two strong links in the diagnosis when other physical signs in heart and lung are negligible.

The abdomen may show distention. The liver often is tender and slightly enlarged. There may be slight muscle spasm in epigastrium or right hypochondrium. Too little consideration given to history and to slight cardiac and pulmonary signs, as just described under these headings, leads to the erroneous diagnosis of some acute abdominal condition, with subsequent negative exploration by a surgeon.

Soon after the infarction occurs slight fever (101°-102°) and slight leucocytosis (10,000-15,000, occasionally 20,000) are almost invariably found. If this is not kept in mind, the fever and leucocytosis may mislead the physician into an erroneous diagnosis of some infectious process with abdominal pain, fever and leucocytosis; an acute inflammatory lesion within the abdomen is simulated and hence the wrong diagnosis and useless operation may follow.

Arrythmia has been referred to already as being present in a majority of the patients. The type of arrythmia is various but no form of arrythmia is in any way characteristic or pathognomonic of cardiac infarction. In many patients the electrocardiogram does show changes in the form of the ventricular complexes, which are almost pathognomonic of the condition and when available electrocardiograms are of much aid in the diagnosis. However, it is to be remembered that the electrocardiogram may be entirely normal in patients with cardiac infarction and hence normal electrocardiographic findings by no means justify discarding the diagnosis of cardiac infarction when the history and other findings point to it. As already emphasized, the correct diagnosis usually can and should be made without the aid of the electrocardiogram. Consequently, I am not going to burden this audience of clinicians with any detailed description of electrocardiographic findings in cases of cardiac infarction. I would add too, by way of advice, in case the obtaining of an electrocardiogram involves transportation of the patient; postpone it until the patient's condition has greatly improved, for rest is more important to the patient than an electrocardiogram. A live patient with a probable diagnosis of cardiac infarction is by far preferable to a dead one, definitely diagnosed by finding a typical electrocardiogram, and the moving of the patient may make the difference between recovery and death.

Treatment, in essential, consists in easing the terrible pain and protecting the heart from the effects of strain. For pain there is nothing so effective as morphia given promptly and repeatedly until one gets its full effects. With severe pain give ½ grain (30 mg.) at once and repeat in ¼ grain (15 mg.) doses until pain is eased. These patients tolerate large doses of morphine. Nitroglycerine is of no effect on

this pain and with the lowered blood pressure is contraindicated. As to the heart, remember that part of the heart muscle has been cut off from its circulation and will die. What remains in good nutrition must carry on heart work. So reduce to a minimum all physical exertion of any sort. Absolute rest in reclining posture is essential. In recovering cases my rule has been six weeks completely in bed and then a very gradual return to physical exertion. The blood pressure level is a very good guide; so long as it remains at a lowered level, great caution in allowing bodily exertion is indicated.

How about cardiac drugs? My judgment is against the use of digitalis, except in patients with a preceding cardiac insufficiency, unless definite signs of decompensation are in evidence during the period of recovery. I have carried some very desperate cases through to complete convalescence without any digitalis. However, this is a matter on which opinion differs and others recommend the use of digitalis. With failing pulse and evidences of cardiac collapse, caffeine in doses of 5 to 10 grains (0.3 to 0.6 gm.) intravenously or intramuscularly, has seemed to me to be by far the most effective drug. This should be repeated as indicated by the evidences of feeble pulse and its response to the drug. In the presence of very grave circulatory failure or cessation of pulse beats epinephrin, administered intravenously or intracardially, is indicated and may tide over the crisis. The dose should be ¼ of 1 c.c. of 1:1000 solution. In my opinio. unusual clinical acumen is required in these cases to determine when and how much cardiac stimulation is needed. My feeling is that more often too large and too frequent dosage with digitalis, caffeine, epinephrin, etc., is employed and that on the whole these patients do best when treated with great conservatism so far as so-called cardiocirculatory stimulants are concerned. Some will die, whatever you do, because the heart is mortally wounded with the first block that occurs in the coronary vessels; others have but a small area of muscle involved and will almost surely recover. Between these extremes lies a group in which much depends on the clinical judgment of the physician in charge, who may err either on the side of doing too much or too little or who may hit the happy middle course of just the proper therapeusis.

Is cardiac infarction a condition of frequent enough occurrence to be of importance to the practicing physician? I think it is. I have had on my service at the Peter Bent Brigham Hospital in a little less than ten years 45 fatal cases and 25 cases that recovered from the attack. Of the latter one may question the diagnosis in all, if one is critical. Among the fatal cases, 28 were proved by autopsy. So you see this is not a very unusual condition within the hospital walls. Many patients are too ill or live too short a time to be sent to the hospital, and so those coming to the hospital are decreased in number by these causes.

So I am inclined to think that it is by no means a very infrequent disease among patients over forty years of age, and so it is a condition of considerable practical importance to know about and to recognize.

In closing I wish to revert to my opening statement that fourth-year medical students of today consider cardiac infarction in rendering a diagnosis on patients assigned to them for history and physical examination and adopt it or eliminate it with a very considerable degree of accuracy. It has seemed to me that these fourth-year students quite often correctly diagnose cardiac infarction when the referring physician has had no idea of what was the cause of the disability that leads him to send the patient to the hospital. Since the diagnosis, as indicated above, is based on very simple clinical methods, available by any physician at the patient's bedside, one is forced to the conclusion that the difference lies in the fact that the student knows of and understands the condition and appreciates that its occurrence is frequent enough to justify consideration in making a diagnosis, while the practicing physician does not. It is this impression that has led me to think it worth while to present this topic before your Association.

REMARKS UPON THE MANNER OF DEATH IN CORONARY THROMBOSIS*

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PROVIDENCE, R. I.

A LARGE percentage of the patients with coronary thrombosis die as a result of that condition. Death is frequently sudden and often occurs when the general condition has improved and the patient seems on a fair way to recovery. In a series of twenty cases, observed in private practice and followed until their termination, eleven died. Seven of them died suddenly and four more gradually. The shortest time from onset until death was about two hours; the longest, four years. Of the seven sudden deaths, the condition just before the moment of death justified a hopeful prognosis in all of them and especially so in five. Of the four gradual deaths, in only one of them was there any abatement of the symptoms after the onset or reason to expect anything but fatal issue.

It is always an interesting question as to what is the mechanism in these cases which causes the heart to cease beating. Were an autopsy available and could a graphic record be obtained just before and at the moment of death, the mechanism in most cases could be demonstrated. The autopsy alone will not reveal the rhythm prevailing at death. A coronary thrombus with an infarct has been considered at autopsy as a sufficient cause of death. However, the mechanism of death is not revealed by the presence of an infarct. If we apply the knowledge gained through graphic methods and animal experimentation, we may, by careful clinical observation of the manner of death, reach a tolerably correct interpretation of the character of the disturbance which with such dramatic suddenness stops the circulation.

The deaths which occur as a result of coronary thrombosis may be divided into three groups.

1. The first includes those cases in which the immediate cause is more or less remote from the original lesion. Not infrequently after an artery becomes occluded an intracardiac thrombus is formed at the site of the infarct. If this thrombus becomes loosened, some disturbance of the circulation occurs. If it is in the right heart and the main pulmonary artery is completely occluded death immediately ensues. If the embolus lodges in one of the branches, any degree of disturbance of the pulmonary circulation may occur. This will depend on the size of the vessel obstructed. If in the left, the result here too depends upon the size of the embolus and the artery which it finally occludes. The most serious ob-

*Read at the meeting of the Association of American Physicians at Washington, D. C., May 5, 1925.

structions are those involving one of the main coronaries, some of the cerebral arteries causing paralysis, the arterial supply of an extremity resulting in gangrene, plugging of the renal artery or any large branch leading to any important organ. Death in the above group of cases is not strictly speaking a cardiac death.

2. In the second group the damage to the heart as a result of cutting off its blood supply may lead to progressive weakening of the heart muscle so that death occurs as it does in any other instance of gradual myocardial failure, or there may be sudden rupture of the heart wall.

3. We may include in a third group those cases in which the heart ceases to beat because of some interference with the mechanism by which the heart beat is maintained in its orderly sequence and efficiency, resulting, e.g., in heart-block or ventricular fibrillation.

CHIEF CAUSES OF SUDDEN DEATH

The chief causes of sudden death are heart rupture either because of a softening infarct or a ventricular aneurysm; embolism of the pulmonary artery; ventricular fibrillation; and heart-block. Whether death occurs as the result of vagus inhibition, so emphatically insisted upon by Sir Clifford Allbutt, is a question very difficult of demonstration. This much may be said that most of the sudden or instantaneous deaths are unaccompanied by pain.

The importance of ventricular fibrillation as a cause of sudden death is not very generally recognized. In experimental observation it has long been noted as the terminal event and especially when a coronary or some branch is obstructed. The first disturbance may be manifest as ventricular extrasystoles, followed perhaps by ventricular tachycardia, culminating finally in ventricular fibrillation. Lewis suggests that sudden death resulting from this abnormal rhythm may sometimes be due to the occlusion of vessels supplying relatively small or deeply seated areas of heart muscle, which remain undiscovered even at autopsy. Obstruction of a small branch may or may not be fatal to an otherwise healthy animal. It is known to be not always fatal in man as shown by fibrotic patches apparently of long standing, found at autopsy.

Very significant is the recently published experimental work of Gold.* He reports a total of fifty-eight ligations of one of the coronaries or of some branch and in more than 50 per cent, ventricular fibrillation developed. In his experiments, too, the effects of ligation in different parts of the coronary circulation varied widely, probably depending upon the amount of compensatory circulation.

Heart rupture and pulmonary embolism may be demonstrated postmortem. It is a difficult matter to demonstrate with certainty that heart-block has or has not been the cause of death and as for ventricular fibril-

*Gold, Harry: Action of Digitalis in the Presence of Coronary Obstruction, Arch. Int. Med., 1925, xxxv, 482.

lation, it leaves no evidence whatever after death as to whether or not it has been present.

In this series there have been no autopsies, but only cases have been considered in which the clinical course leaves little or no doubt that the condition was coronary thrombosis. In two of the cases, the weight of evidence seems in favor of the opinion that death occurred from heart block. Three others died while lying in bed without a moment's warning. Two others died on the seventh and ninth day very abruptly. They had been desperately ill and had greatly improved until the day of death. On that day there was a slight recurrence of the pain and discomfort lasting for a few hours and this was followed by an abrupt termination.

Another was sitting on a bench at the Country Club two hours after the onset discussing whether to attempt to get to his home or to wait a few minutes until he should feel better. He fell over unconscious and died at once.

One died in great pain with a gradually failing heart four hours after the onset. One died thirty hours after onset with gradually developing edema of the lungs. One other died twenty-one days from the onset with recurrence of symptoms on the thirteenth day. Tachycardia developed on the seventeenth day lasting four days until the heart ceased from exhaustion.

The details of some of these deaths are rather interesting. Four in the acute stage happened in much the same manner. All had passed the stage of pain. One who had been restricted with the greatest care had reached the fourteenth day. In the night, while he slept, the nurse who sat at his bedside noticed a sudden change in his breathing. She tried at once for his pulse which was imperceptible. He gasped a few times and was dead. This patient had had three attacks of auricular fibrillation varying in length from two to sixteen hours each during the time of his illness. They had made him a trifle uncomfortable but had not inconvenienced him seriously. The pulse rate during the fibrillation was not very rapid, about 120.

Another suffered agonizing pain for the first couple of days and developed considerable fever. In a few days the pain and fever subsided and he was quite comfortable. He was using great care to avoid exertion. On the seventh day he felt so well that he insisted on seeing his secretary. While lying flat in bed giving her some directions he suddenly became cyanotic, gasped a few times, and died.

A third complained of such pain on the first day that he said if not relieved he knew he could not live. On the second day there was a pericardial friction sound. He then gradually improved and reached the ninth day and was beginning to ask for the privilege of sitting up when on the afternoon of that day he had some recurrence of the pain. This was relieved in a few hours and he was talking with his wife as to the

chances for his recovery and about some of their plans. In less than a minute from the time they finished talking he was dead.

A fourth, also desperately ill at the onset, had shown much improvement and had reached the seventh day of his illness. He had a very comfortable afternoon. Upon awakening from a nap he complained of not feeling quite so well and died in about twenty minutes. In this instance there were premonitary symptoms at the end. Had there been an opportunity for observing the pulse or listening to the heart beat it might have been possible, perhaps, to determine what disturbance of rhythm, if any, was occurring and in that way to have obtained a clue as to what happened.

Of the two cases which seemed to die from heart-block one was ill for four days only. He was desperately ill from the start and there seemed little chance for his recovery. A pericardial friction sound developed on the second day. His pulse was extremely variable, from 40 to 120. At times it could not be felt. During the last day he had numerous convulsions. The nurse described one of these convulsions as follows, "The pulse was very slow for a few seconds, then could not be felt at all, and then the patient became rigid, the pulse remaining absent for a short time, then it reappeared increasing in rate to about one hundred." He finally died in a convulsion. These were probably recurrent attacks of Adams-Stokes' syndrome. The other patient, to whom it seemed reasonable to assign heart-block as the cause of death, died two and one-half years after the coronary occlusion. The onset was complicated by pulmonary signs and the condition at the time was considered to be bronchopneumonia. One month after the onset an electrocardiogram was taken which showed the characteristic V-shaped T-wave. The electrocardiogram was repeated during the next four months and by that time the T-wave had returned to normal. The patient was not seen then for some time. Two and one-half years later he was in the country one Sunday afternoon working about his place when he had a fainting attack. According to friends who were with him he had a convulsion and was unconscious for a time. He was able to get back to the city and when seen that night at nine o'clock seemed quite himself although he complained of having bitten his tongue. He was advised not to go to business for a few days. He got up the next morning as usual, dressed, had breakfast, and went to the telephone to say that he would not be at his office that day. While telephoning he fell dead. The attack on the previous day in this case could hardly have been either ventricular fibrillation, pulmonary embolism, or ruptured heart. It might have been heart-block with a resumption of the rhythm, and a reasonable supposition would be that the same cause was operating the next day, this time resulting in death.

Another case, seen by the writer at the moment of death, had had some attacks of angina, but not serious ones. He had this final attack while

at the Country Club where he had been for lunch. He, at the moment, was sitting on the bench discussing whether he felt well enough to come to the city when suddenly in rather a startled tone he exclaimed, "I feel faint." He fell over at once unconscious. His pulse, which had been of good character up to that moment, could not be felt. There were a few convulsive movements during which there appeared the most extraordinarily rapidly developing cyanosis and the patient was dead within a fraction of a minute. It is quite a matter of conjecture which of the four usual causes of sudden death operated in this case. From the history the least likely cause would seem to be heart rupture or a pulmonary embolus. The great suddenness with which the pulse disappeared with no previous change in the rhythm suggests fibrillation as the greatest probability.

One very interesting case from the point of view of prognosis may be mentioned. A man of forty-six, foreman in a mill, who gave a characteristic history of an attack of coronary thrombosis, was seen in the office a month later where a confirmatory electrocardiogram was obtained. He was not seen again. However, it was learned that he had in the course of a year apparently quite recovered and had gone back to his original work, that he seemed to be as well as ever and that he would take Sunday walks of four or five miles with comfort. About a month before he died—four years after the onset—he had been apparently as well as usual on that day and went to bed seeming perfectly well. Soon after going to bed his wife noticed some peculiarity in his breathing, turned on the light, and found that he was dead. I have seen, at least I have recognized, no other case of such long duration.

Another type of death is illustrated by a patient who lived for twenty-one days. At the onset it seemed like a rather mild attack of angina pectoris, unusually resistant to morphine. There was considerable improvement for a week and then a pericardial friction sound was discovered, possibly from some further infection. On the seventeenth day he developed a tachycardia at the rate of about one hundred and fifty, which persisted for four days, death occurring finally from cardiac exhaustion.

It is perhaps dangerous to form conclusions without any more positive data than can be given in such a series of observations. On the other hand, it may be profitable to give one's impressions. As stated in the beginning, it is difficult to prove which is the faulty mechanism at the end. Those of us who have had considerable autopsy experience know that a ruptured heart is very infrequently seen. It is also true that an embolus sufficiently large to block the main pulmonary artery is rarely found in this condition at autopsy. That leaves for consideration ventricular fibrillation, heart-block, and the possibility of death from vagus inhibition. The main bundle of the conducting system has its own blood supply, usually a branch from the right coronary and if this vessel should be involved, heart-block would likely occur. Finally, when one considers the rarity of thrombosis of the right coronary and the comparative fre-

quency with which ventricular fibrillation occurs when an artery is experimentally occluded, there would seem good reason for believing that ventricular fibrillation is the most common cause of sudden death in this condition.

This mechanism may also be the explanation of many cases of sudden death which occur without any previous warning symptoms. Experimental work has shown that ventricular fibrillation may develop quite soon after the coronary vessel is obstructed. In those cases of sudden death in which there has never been any demonstrable signs or symptoms of cardiac disease it may be that a small deep seated sclerotic vessel becomes occluded without causing any symptoms before the onset of fibrillation. In those cases which seem to be having very satisfactory convalescence following coronary thrombosis but which suddenly die it is possible also that the ventricle is excited into fibrillation by the extension of the thrombus into a new area. This explanation is supported by the fact that in some instances there has been a short period preceding death during which the patient complains of discomfort or in general of not feeling quite so well.

VASODILATATION FOLLOWING SYMPATHETIC NEURECTOMY*

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THE profession is indebted to Maurice Raynaud, to Weir Mitchell and to Buerger for the three classical studies which have made possible the differentiation of the various vascular and vasomotor diseases of the extremities. Buerger's recognition of a new entity, thromboangiitis obliterans, has markedly simplified diagnosis in what has been hitherto an extremely difficult field.

In the Mayo Clinic a special section on medicine has been assigned for the study and care of vascular diseases. Patients with vascular disease are placed in a hospital and, even if this disease is surgical in nature, they are supervised by the medical staff before and after operation. Through the cooperation of the Section on Physics special facilities have been provided for calorimetric studies, the measurement of heat production and radiation in the extremities, and for recording skin surface temperature. The color of the skin, the capillary reactions and the changes in the volume of the blood have also been studied. Capillary microphotography has been perfected to the point of being clinically applicable.

In the earlier period of our work, the treatment of thromboangiitis obliterans was attempted on medical lines and consisted of (1) the administration of vasodilating drugs such as nitrites and citrates, (2) the daily administration of 6 to 12 liters of Ringer's solution as suggested by McArthur, and (3) the prolonged application of moderate heat, the employment of contrast baths, postural exercises and so forth. In Raynaud's disease, and allied vasomotor disturbances, vascular reeducation was attempted through forms of hydrotherapy and body air baths, alternate use of hot and cold showers, foot plunges, and so forth. But the results of medical treatment were not entirely satisfactory and the surgeons were requested to participate in treatment in the hope that, through surgical procedures, relief from pain might be secured. Our cases fall logically into two series: those in which the Leriche-Handley operation was performed and those in which sympathetic neurectomy was performed.

During the last three years, approximately fifty patients with Buerger's disease have been admitted to the hospital and studied.

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About half the patients were Hebrews. In one-third of the patients, the upper as well as the lower extremities were affected. A true instance of this disease was encountered once in a woman. The age incidence varied from seventeen to forty-eight years.

THE RESULTS OF THE LERICHE-HANDLEY OPERATION

Organic Obliterative Group.—In our first series of cases, twenty-four Leriche-Handley operations were performed on seventeen patients. This operation consists of stripping the adventitia from the vessel for a distance of about 2.5 cm. after its injection with 95 per cent alcohol. The results in Buerger's disease were practically negligible in all except one case. This was the case of a young man in whom all four extremities were affected but in whom there were superimposed vasoplastic phenomena suggesting those observed in Raynaud's disease. The operation was performed on the right arm and right leg. Decided benefit resulted from the standpoint of relief from pain. Subsequently, the disease progressed on the left side to the point where, on the patient's return to the clinic, amputation of the leg was necessary. The condition of the right leg continues to be satisfactory after twenty-eight months. Calorimetric studies with the Stewart-Kegerreis calorimeter, however, failed to demonstrate changes in the production of heat.

The gross appearance of the femoral and brachial arteries in thromboangiitis obliterans was fairly characteristic. Some degree of periarterial inflammation, with infection of the adventitial fibrous network, was observed in every proved case. The inflammatory periarteritis made the dissection of artery from vein difficult. This was not observed in the arteriosclerotic type of vessel.

Operations in three cases of endarteritis obliterans failed to accomplish anything. Because results were not satisfactory, the Leriche-Handley operation has been abandoned in the obstructive type of vascular lesion.

A unilateral operation was performed in one case of erythromelalgia. The condition had lasted twenty years and the symptoms were so severe that in order to avoid the pain which resulted from walking, the patient had crawled on hands and knees for several years. The operation brought no relief. The perivascular injection of alcohol in a second case also failed to relieve.

Vasomotor Group.—The first series also includes two cases of Raynaud's disease which were subjected to the same procedure. At operation no demonstrable periarteritis or changes in the gross appearance of the exposed vessels were observed. In the first case the result was negligible. In the second, bilateral operations were performed on the arms with excellent results on the left and failure on the right.

The nature of the results in each instance were immediately apparent. On the left side cyanosis promptly disappeared at room temperature and the attacks of tingling and burning were also relieved. Fig. 1 indicates the heat curves of the left hand before and after operation. A comparison of the postoperative heat curves taken at intervals of three days showed that the period of maximal vasodilatation occurred in from five to eight days. Two weeks after operation there was a decrease, and the values were about the same as before operation.

The surgeon ascribed the failure of results in the right arm to the fact that the breaking of a small arterial twig necessitated ligation which mechanically or through reflex irritation stimulated the vessel wall to vasoconstriction at this point. During the operation and following ligation of the twig, a marked spasm of the brachial artery occurred and persisted for several hours. Pulsations were not felt in

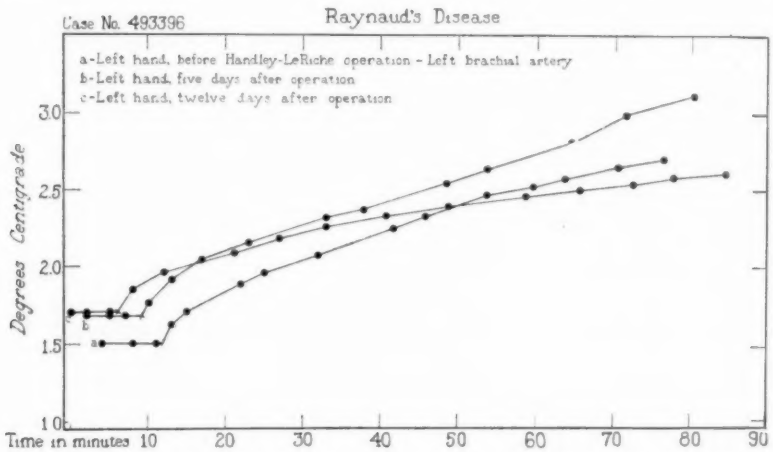

Fig. 1.—Heat curves showing slight increase in heat production and radiation of the left hand after operation.

the radial artery. The contraction was distinctly segmental, involving about 2.5 cm. of the vessel (Fig. 2). The spasm was not intermittent, the contracture persisting continuously during the twenty minute period of observation. Five hours later normal radial pulsation was observed. The patient is highly gratified so far over the results obtained in the left arm.

The Hypertension and Nephritis Group.—During the course of these studies it occurred to us that relief from hypertension might be attained through the release of the vessels of an extremity from sympathetic vasoconstriction. Consequently a Leriche-Handley operation was performed under local anesthesia on the left femoral artery in Scarpa's triangle of a patient suffering from marked hypertension, chronic nephritis, arteriosclerosis, and terminal uremia. The course of the disease was in no way affected, and no significant change in the

general blood pressure or that in either extremity could be determined. It was felt, however, that this was hardly a fair test since the patient was not far from moribund at the time of the operation.

THE RESULTS OF LUMBAR SYMPATHETIC NEURECTOMY

Calorimetric Studies in Spastic Paraplegia.—Physiological studies to determine the vasomotor effect of bilateral lumbar sympathetic neurectomy have been carried out in a group of cases of spastic paraplegia and form the basis of a separate study. In a group of five patients with

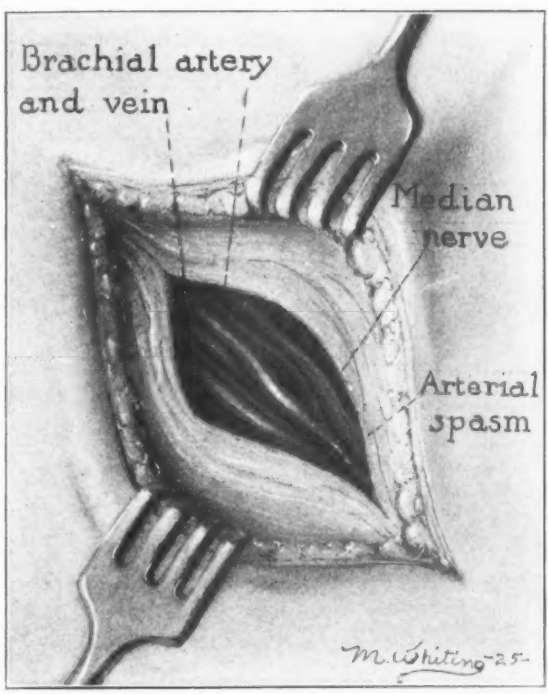

Fig. 2.—Spasm of brachial artery during operation.

spastic paraplegia in whom lumbar sympathetic neurectomy through the abdominal route was performed, careful clinical observations were made, the temperature of the skin was determined, the capillaries were studied, and the heat production and radiation were determined by the Stewart-Kegerreis calorimeter before and after operation (Fig. 3). After operation it was found that heat production and conduction in the feet were increased by from 200 to 900 per cent. There was an increase in the temperature of the skin of the feet of from 2 to 6° C. In the preoperative determinations of the temperature of the skin, the normal decrease in the temperature towards the periphery was observed. Following operation the reverse was noted and the

feet became relatively warmer. The skin was strikingly dry and there was no sweating. The skin of the feet became scaly, and in one case partial skin casts of the soles of the feet were exfoliated. The color changes were slight and were not invariably present. They consisted of rubor along the toes and the margins of the feet. The subjective sensations in the most striking cases were similar to those experienced in cases of mild erythromelalgia. Burning sensations, aggravated by heat and relieved by cold, and dryness of skin were marked. Muscle cramps were complained of in two cases.

The vasodilatation, following the removal of the second, third, and fourth lumbar ganglia with the sympathetic trunk and the division of the rami, suggested the application of this procedure to the treatment of vasospastic conditions such as Raynaud's disease, and a bilateral

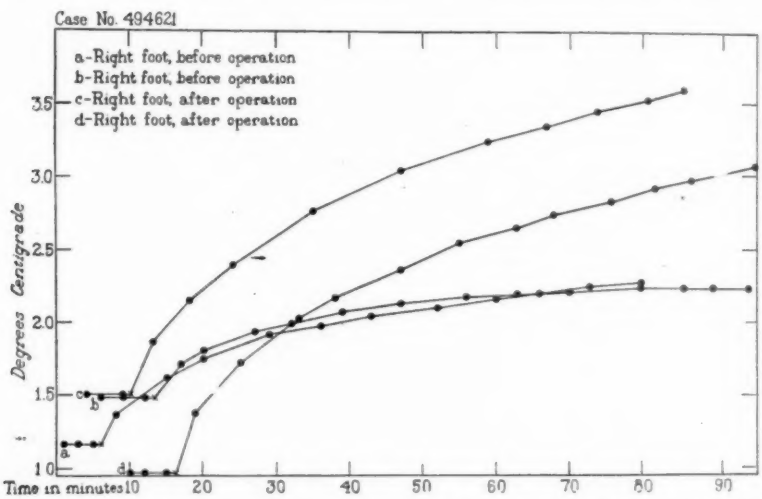

Fig. 3.—Heat curves showing increased heat production and radiation of the foot following operation.

lumbar sympathetic neurectomy, with stripping of the adventitial coat of the common iliac artery, was performed on a patient with well-defined Raynaud's disease of the feet. Calorimetric studies following operation showed that vasodilatation had occurred; the vasomotor phenomena disappeared and the superficial ulcers of the skin healed rapidly. This case, and one in which cervical sympathetic neurectomy was performed for Raynaud's disease of the upper extremities, will be reported elsewhere.

Malignant Hypertension.—The application of sympathetic neurectomy in the treatment of hypertension was considered. We believed that this might not only lower systemic blood pressure but provide an area of diminished resistance which would give way under strain for the protection of cerebral and retinal vessels. Although no demon-

strable effects on systemic blood pressure have been observed in the normal pressure cases in which sympathetic neurectomy has been performed, it seemed possible that if the hypertension were marked there would be a certain reduction of systemic blood pressure. The case reported here represents an example of early malignant hypertension of the group such as has been described by Wagener and Keith.

REPORT OF A CASE*

A man, aged thirty-three, was admitted at the Mayo Clinic, November 19, 1924, complaining of blurring of vision and headache. He had had acute rheumatic fever in 1917, and influenza in 1918. His increased blood pressure was discovered in

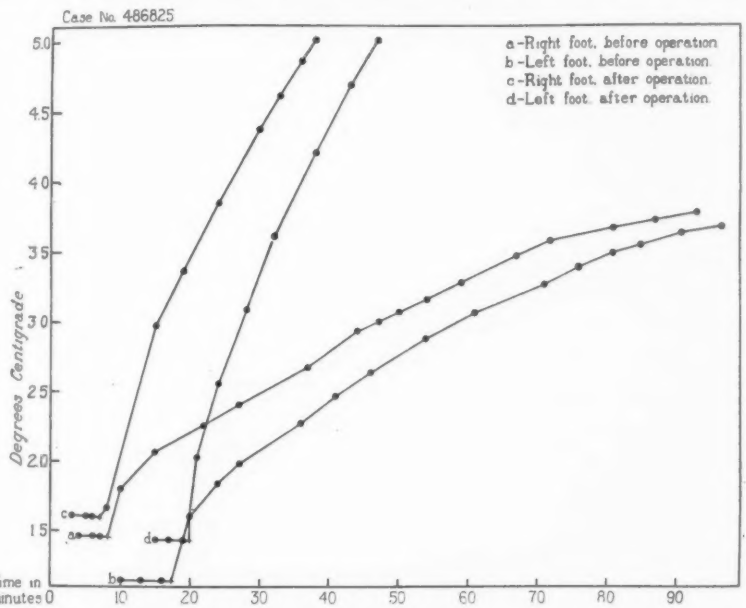

Fig. 4.—Heat curves showing marked increase of heat production and radiation in the foot following operation.

1919, at which time the systolic pressure was 190 mm. The following year he suffered from occipital headaches, nausea and vomiting, most marked in the forenoon. In March of this year his vision began to fail and he noticed increasing blind spots in each eye.

On admission he weighed 185 pounds. The peripheral vessels were moderately sclerosed and the heart slightly enlarged. The systolic blood pressure was 230 mm., the diastolic 130 mm. There was slight edema of the discs, cotton-wool exudates and hemorrhages involving the left macular region, with contraction in the retinal arteries. The renal function was excellent. The electrocardiogram showed no significant changes. Our diagnosis was early malignant hypertension. The patient was admitted to the hospital, but he did not respond at all well to the routine treatment, rest, nitrites and hydrotherapy. Because of the absence of marked organic changes the possibility of relief by abdominal sympathetic neurectomy was discussed

*The studies of the blood pressure and calorimetric data in this case will be included in a separate report.

with him. As he was very anxious to have any procedure tried, even if admittedly experimental in nature, the operation was performed. His average systolic blood pressure under medical treatment ranged from 170 to 200, and the diastolic from 90 to 130. When he came to the operating room the systolic blood pressure was 255, the diastolic 90. The second, third and fourth lumbar segments of the sympathetic chain were severed, together with the ganglia, and the rami.

The patient's recovery was uneventful. The day following operation he complained of a sensation of heat and burning in the feet and legs. These were dry and red, especially on the soles. The skin became dry and scaly. Skin temperature determinations were carried out, and it was noted that the temperature was very definitely increased in both feet. Calorimetric studies of heat production by means of the Stewart-Kegerreis calorimeter showed an increase of 300 per cent in heat production and heat radiation (Fig. 4). The blood pressure level was distinctly lowered. Two weeks after the operation the headaches had disappeared, and vision had improved materially so that the patient could read almost any print with comfort. While he was up and about, the blood pressure gradually mounted. His response to nitrites and hypertension baths was much better than before the operation. A letter received four and one-half months after operation expresses great satisfaction over the subjective improvement. Six months after operation his blood pressure, taken by his local physician, was 220 systolic and 120 diastolic. Headache occurred occasionally.

While the outcome of this operation was not entirely satisfactory yet there was definite subjective and objective improvement. The patient has worked continuously, and without discomfort since his return home, although he had been entirely incapacitated prior to coming to Rochester. The time elapsing is too short to form a final conclusion concerning ultimate results.

THE EFFECT OF SLEEP ON NORMAL AND HIGH BLOOD PRESSURE*

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IT is commonly accepted as fact that blood pressure in man is so variable that single and isolated observations often lead to wrong conclusions. Granting that methods now practiced are accurate, we must make many allowances for physical, psychic and metabolic activity before we can estimate from blood pressure what work the heart is doing or what stress the vascular structures must bear. These variable factors are most constant in sleep, and sleep comprises one-fourth to one-third of our entire living, but very little is known of the normal blood pressure in sleep and even less of pathological blood pressures. Mechanical difficulties alone interfere with practical measurement of the blood pressure in sleep, for such investigation as has been done shows that the practice does not necessarily interrupt natural sleep, nor is it apparent that when partial or transient waking is produced, blood pressure changes before a reading can be made.

Leonard Hill,[5] studying the blood pressure of a normal young man during sleep, using his own apparatus and recording mean blood pressure, as estimated from maximum oscillations, determined that there was little if any change of blood pressure caused by falling asleep. Quite different observations were made by Brush and Fayerweather[4] in 1904, who used a plethysmograph method in a greater number of subjects. They found a substantial fall of blood pressure in the first two hours of sleep followed by a continuous rise as sleep was prolonged—going to a point higher than before sleep appeared. We find much difficulty harmonizing their reports with any subsequent work because it deals with the so-called "mean pressure."

Brooks and Carroll[3] in 1912 recorded the true systolic pressure of 30 normals but it does not appear in their reports just how frequently and how regularly readings were made. It is quite certain that the first two hours of sleep were those most studied—which puts some doubt on the value of their conclusions that the blood pressure is lowest in the first two hours of sleep.

Our own observations include both systolic and diastolic pressures, as recorded by an apparatus of original design described by one of us (M. A. B.)[1] and somewhat further developed by the other. This apparatus since its original description has been improved by an automatic

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release, which prevents unnecessary compression of the arm after diastolic pressure has been recorded, thus permitting more uninterrupted sleep. A further improvement in technic has developed from a better understanding of oscillometer tracings. Practically all records now can be read for systolic and diastolic pressures. The diastolic is especially distinct when the tracings are viewed almost parallel to the line of vision. With the waves thus foreshortened, the peaks can be seen forming a line which follows a definite course with the increment and decrement of oscillation, but the decrement is not absolutely uniform and a break in the line representing a decrease in the decrement has been found to correspond to the diastolic pressure. That such is actually the case in each subject studied was determined by listening in with the stethoscope while preliminary tracings were being made. By a signalling device the Korotkoff sounds can be accurately located on the oscillometer tracing and the criteria thus compared directly.

With this equipment 25 normal young men were studied when just about to be discharged from hospital after minor ailments. They were put back in bed and kept continuously at rest for the experiment, so that aproximately basal conditions obtained. Continuous records were not made during the day, and all feeding and other activity necessary to care limited to the day. From twelve to twenty-four hourly records were made by the automatic device and the sleeping state was recorded by a nurse. These records are averaged and arranged with reference to the act of falling asleep and of waking, so that the arrangement constructs a curve.

While not all of the 25 slept exactly eight hours, the curve (Fig. 1) represents the exact average of 25 in the sleeping and waking periods. But the middle portion of the sleeping curve is, therefore, an average of less than 25.

In nearly every case the position of the patient at the moment of registration was noted to determine whether he lay on back, right or left side, so that a correction necessary for posture could be applied to the reading. This curve, corrected and uncorrected, shows an abrupt drop in the first two hours of sleep followed by a gradual and continued decline as sleep was prolonged. Accompanying the blood pressure curve is another representing the pulse rate at the moment blood pressure was recorded; this information can be read directly from tracings produced by the instrument. A very striking parallel between blood pressure and pulse rate was noted. It must be remembered that these very low blood pressure figures, 110 waking and 101 sleeping, were obtained under practically basal conditions.

High blood pressure in sleep has been the subject of investigation in at least four instances, viz., by Brooks and Carroll[3]; by Müller[7] in 1921; Blume[2] in 1922, and Katsch and Pansdorf[6] in 1922. In the more recent reports it is noted that some patients experience a

fall of blood pressure in sleep and others do not—but in no report does it appear that methods were elaborated so that records could be made at frequent intervals throughout the night. The general belief that the greatest drop occurs in the first two hours of sleep has prevailed, so that principally that part of sleep has been studied to the exclusion of the rest. From our studies on normals as well as abnormals we are certain that the later hours of sleep are very important

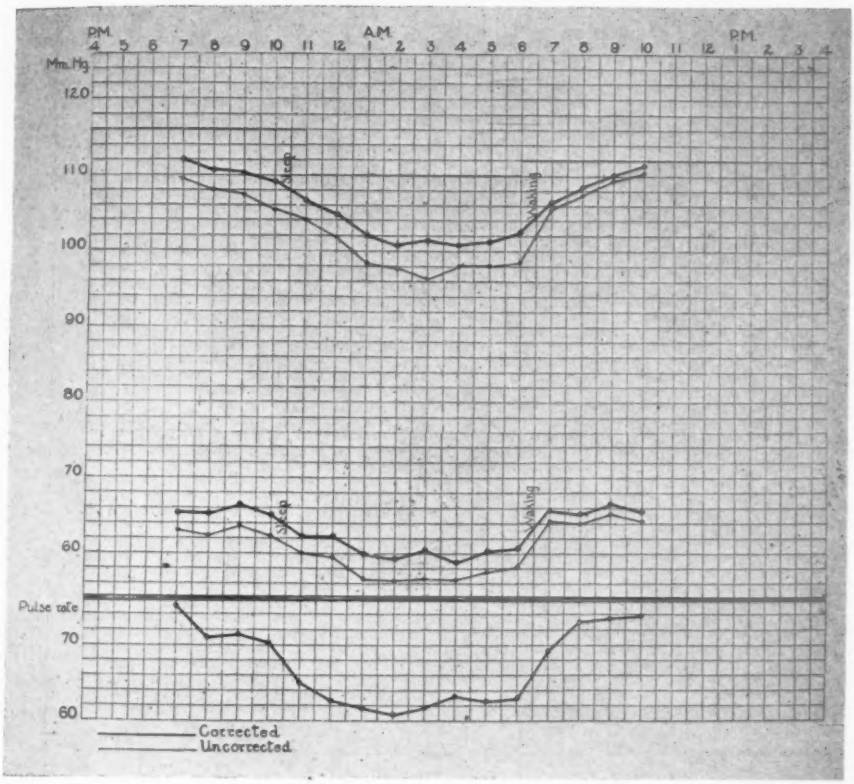

Fig. 1.—Blood pressure and pulse rate by automatic hourly registration of twenty-five normals.

and in light sleepers that the later hours of the night are the most important.

It is surprising and somewhat disappointing that blood pressure records in sleep have been so little used in the clinic when *a priori* they should be so useful. The labor of making such records within the first two hours of sleep is doubtless the greatest reason for their unpopularity. Our studies on the normal as well as on those with high blood pressure show that readings taken any time after sleep is well established should show a fall if the subject be physiologically capable of permitting a fall of blood pressure to occur.

TABLE I

GROUP A. PATIENTS SHOWING FALL IN SLEEPING PRESSURE

CASE NO.	INITIALS	AGE	RACE	SEX	PRESENTING SYMPTOMS	YEARS OF HEART DISEASE	KIDNEY DISEASE	H.B.P.	DEGREE OF NOCTURIA	DEGREE OF DISABILITY	OPTIC FINDINGS	LEFT CARDIAC BORDER FROM MIDLINE	DEGREE OF ARTERIOSCLEROSIS	DYE TEST %	VARIATION IN 2 HR. SP. GR.	ALBUMIN	CASTS	BLOOD UREA	BLOOD CHLORIDE	BLOOD PRESSURE ON ADMISSION	DAYS IN HOSPITAL	PROGNOSIS
12	J.M.	30	W	M	Abd. pain.		4	5	++	+	Small hem.	11 cm.	++	65	12-21	+	Hyal. gran.	56		210/150	15	good
3	A.B.	37	W	F	diabetes	–	–	⅛	–	+	–	12 cm.	–	50	03-21	+	few	18		150/80	12	good
40	T.D.	39	W	M	nocturia	–	?	?	+++	+		norm.	+	45	15-22	+	–	37	36	150/90	4	good
39	R.F.	39	W	F	backache	3	3	3	+	+	–	13 cm.	–	50	12-26	+	H&G	20	42	200/120	5	good
5	C.D.	55	N	F	nocturia vertigo dyspnea	–	–	–	++++	+	tortuous vess.	AAL	+	55	04-30	–	–	40	49	200/130	15	good
75	S.T.	59	W	F	vertigo nocturia	2	–	2	–	+	tort. vess.	12 cm.	+	65	05-15	–	–	21	42	200/110	2	good
28	E.O.	54	W	F	loss wt. abd. pain	–	–	–	–	+	–	13 cm.	+	55	07-26	–	–	26	45	200/120	12	good
7	L.G.	58	W	F	H.B.P. diabetes vertigo	?	?	5	–	+	tort. vess. small hem.	AAL	+	65	12-27	–	–	24	39	240/140	4	fair
14	V.R.	50	W	F	headache vertigo	2	2	2	+	+	tort. vess.	slight enlg.	++	70	01-12	–	few H&G	33	47	210/110	20	fair
29	G.S.	53	W	M	gas ulcer	10	10	10	–	++	–	norm.	++				–	40	44	160/120	30	fair
60	A.C.	66	W	F	headache vertigo	½	8	¾	++	++	tort. vess.	12 cm.	+	30	02-06	+	few H&G	27	44	180/100	10	good
51	J.D.	63	W	M	arthritis emphysema	½	½	½	++	++		14 cm.	++	30	22-28	–	–	37	39	170/90	2	good

TABLE I—CONT'D

GROUP A. PATIENTS SHOWING FALL IN SLEEPING PRESSURE

CASE NO.	INITIALS	AGE	RACE	SEX	PRESENTING SYMPTOMS	YEARS OF HEART DISEASE	KIDNEY DISEASE	H.B.P.	DEGREE OF NOCTURIA	DEGREE OF DISABILITY	OPTIC FINDINGS	LEFT CARDIAC BORDER FROM MIDLINE	DEGREE OF ARTERIOSCLEROSIS	DYE TEST %	VARIATION IN 2 HR. SP. GR.	ALBUMIN	CASTS	BLOOD UREA	BLOOD CHLORIDE	BLOOD PRESSURE ON ADMISSION	DAYS IN HOSPITAL	PROGNOSIS
35	T.C.	46	N	M	blurring vision tinnitus	?	?	½	–	++	–	14 cm.	++	55	01-12	–	–	18	42	225/140	19	uncertain
56	M.C.	60	W	M	diabetes	5?	5?	5?	+++	++	retinitis	13 cm.	++	50		++	few hyal.	51		160/110	15	poor
31	Z.T.	41	W	F	cerebral hemorrhage	–	–	?–	–	+++	–	norm.	–	62	04-20	+	–	19	34	190/120	9	bad
36	M.M.	69	W	M	weakness dyspnea	–	–	2	++	++++	tort. vess.	14 cm.	++	55	08-20	++	H&G	43		190/70	8	poor
27	J.J.	55	N	M	hemiplegia	?	?	?	+++	++++	vess. contracted	12 cm.	++++	45	04-16	–	–	22	47	200/100	16	poor
17	B.S.	56	W	M	renal colic	?	?	?	++++	+++	tort. vess. hemo.	AAL	+	70	04-11	++	H&G	24		200/100	12	poor
16	A.S.	77	W	F	arthritis		14		+++	++++	tort. vess.	AAL	+++	30	12-22	–	few hyal.	24	49	220/120	26	good
26	R.F.	58	W	M	edema acute nephritis	–	–	–	–	+	–	–	–	50	10-16	++	+++	80		130/100	48	good

+ = positive findings.
- = negative history or normal finding.
? = indefinite.
blank = undetermined finding.

TABLE I—CONT'D

GROUP B. PATIENTS SHOWING LITTLE OR NO FALL IN SLEEPING PRESSURE

CASE NO.	INITIALS	AGE	RACE	SEX	PRESENTING SYMPTOMS	YEARS OF HEART DISEASE	KIDNEY DISEASE	H.B.P.	DEGREE OF NOCTURIA	DEGREE OF DISABILITY	OPTIC FINDINGS	LEFT CARDIAC BORDER FROM MIDLINE	DEGREE OF ARTERIOSCLEROSIS	DYE TEST %	VARIATION IN 2 HR. SP. GR.	ALBUMIN	CASTS	BLOOD UREA	BLOOD CHLORIDE	BLOOD PRESSURE ON ADMISSION	DAYS IN HOSPITAL	PROGNOSIS
32	E.H.	50	W	F	diabetes	7	7	7	–	++	–	13 cm.	–	50	08-16	+	–	22	44	240/120	16	fair
62	C.R.	38	N	M	H.B.P.	–	13	13	+++	+	norm.	12 cm.	+	60	20-30	+	–	33	37	190/140	11	good
44	S.S.	53	W	M	failing vision	3	3	3	+	+	tort. vess. hem'ge.	16 cm.	++	40	10-20	++	many H&G	46		240/150	3	poor
15	M.R.	60	W	F	epigastric pain; vertigo	18	4	?	++	+	vess. tort.	AAL	+	60	03-24	–	–	29		300/168	33	uncertain
37	S.R.	36	W	M	cerebral hemorrhage	2	2	2	+	+++	–	11 cm.	+	55	08-20	+	few hyal.	20	42	175/105	9	poor
34	J.F.	56	W	M	headache weakness tinnitus	8	8	8	+++	++	small hem.	13 cm.	++	55	04-16	+	–	37	44	250/130	10	poor
68	C.S.	37	N	M	dyspnea	1	1	1	++	+++	–	11 cm.	+	50	16-23	+	–	20		235/160	21	uncertain
47	J.C.	37	N	M	headache dyspnea	1	1	1?	++++	++++	old hem.	AAL	+++	30	03-11	+	few	37		200/150	20	poor

TABLE I—CONT'D

GROUP B. PATIENTS SHOWING LITTLE OR NO FALL IN SLEEPING PRESSURE

CASE NO.	INITIALS	AGE	RACE	SEX	PRESENTING SYMPTOMS	YEARS OF HEART DISEASE	KIDNEY DISEASE	H.B.P.	DEGREE OF NOCTURIA	DEGREE OF DISABILITY	OPTIC FINDINGS	LEFT CARDIAC BORDER FROM MIDLINE	DEGREE OF ARTERIOSCLEROSIS	DYE TEST %	VARIATION IN 2 HR. SP. GR.	ALBUMIN	CASTS	BLOOD UREA	BLOOD CHLORIDE	BLOOD PRESSURE ON ADMISSION	DAYS IN HOSPITAL	PROGNOSIS
61	C.T.	54	W	F	coma cereb. thromb.	?	?	1	+	++++	tort. vess.	AAL	+	70	26-40	+	few	28	27	200/110	34	poor
13	J.M.	56	N	M	gastric	5	1	?	+	++++		AAL	+++	65	16-22	–	–			230/110	12	bad
9	S.G.	50	W	M	poor vision vertigo	2	2	2	++++	+++	old hemo.	11 cm.	+	25	16-23	+++	hyal.	34		280/130	27	poor
18	M.T.	48	W	F	dyspnea	?	4	4	+++	++++	old hemo.	MAL	+	?	18-22	+++	H&G	42	39	215/110	39	died
30	R.S.	40	N	M	edema	2	2	1	–	++++	tort. vess.	AAL	++	30	10-18	+++	H&G	43	52	190/100	43	died
38	O.W.	57	W	M	edema dyspnea	18	2	2	+++	++++	–	15 cm.	++	40	16-30	+	many H&G	28	47	175/130	50	died
10	W.J.	22	N	F	edema nocturia acute nephritis	3	3	3	++++	++++	–	11 cm.	–	35	10-12	+++	many hyal.	85	56	200/110	64	died
21	L.S.	28	N	F	weakness dyspnea acute neph.				+++	++++	retinitis	17 cm.	–			+++	many gran.	171	73	280/160	9	died

\+ = positive findings.
\- = negative history or normal finding.
? = indefinite.
blank = undetermined finding.

Thirty-six patients in hospital, with high blood pressure, were studied by hourly automatic registration in the same manner as the twenty-five normals cited above. A few were observed for but a single night, but the majority were repeatedly observed, and the entire record tabulated for purposes of study. Unless the patient willingly tolerated the tests and agreed that the testing did not interfere with sleep his record was not included in the report. A few such subjects were rejected as unsuitable for study—either as too ill, too nervous or suspicious of experiments. All were studied and recorded by the usual technic as to physical description, urinalysis, blood analysis and kidney function tests, together with a blood pressure record made in the ordinary manner sometime during the first hospital day.

Table I is a tabulation of all the data thus obtained. For comparison the entire group has been arbitrarily divided into two subgroups: Group A whose average minimum systolic pressure in sleep is below 100 plus the patient's age and is presumably normal; Group B whose average minimum sleeping pressure is above this arbitrary standard and, therefore, is abnormal.

We could not construct a curve showing the effect of sleep on high blood pressure after the manner of the twenty-five normals. All degrees of high blood pressure are represented in this study together with all degrees of sclerosis, nephritis and heart disease. In this heterogeneous class, blood pressure curves of all variety are found so that graphic generalization is impossible.

In general there is greater variation from hour to hour in both the waking and the sleeping states than is seen among normals. There is also less total sleep and less uniformity of the hours of sleeping and waking, due no doubt to the fact that all patients in this group were ill.

Contrary to the findings of Brooks and Carroll our patients showed a fall of blood pressure in sleep inversely proportional to the waking pressure—that is, the higher the waking pressure, the less the fall due to sleep. Only one, No. 40, showed a sleeping pressure (90-55) which could be called normal by the standard we have established. Every patient in the entire group showed some fall during sleep when the average waking pressure was compared with the minimum sleeping pressure. When the average hourly waking pressure was compared with the average hourly sleeping pressure, the fall in all cases is less, and in some instances there is absolutely no difference—that is, no fall during sleep.

The greatest contrast is seen when the maximum waking pressure is compared with the minimum sleeping pressure. This was for the two groups as follows:

Group	B	A
Average of all days		
Maximum waking systolic	232	192
Maximum waking diastolic	140	114
Average of all nights		
Minimum sleeping systolic	195	132
Minimum sleeping diastolic	109	79

Considering all of the data of Table I, with the cases grouped thus, we see more than anything else that the group B, showing little or no fall, had more evidence of disease, greater disability, stayed longer in the hospital, and had higher day pressure. Group A had less evidence of disease, less disability, stayed shorter time in hospital and had less elevation of blood pressure.

SUMMARY

Twenty-five normal young men at basal conditions showed a drop of blood pressure from 110 to 101 by falling asleep.

In normals the greatest drop, due solely to sleep, comes at about the fourth hour of sleep, but this lower level continues throughout the sleeping state. There is a slowing of pulse in sleep parallel to the drop in blood pressure.

Of thirty-six patients with elevated blood pressure, but one showed a normal fall of blood pressure in sleep. Sixteen showed a fall due to sleep, which reached a level regarded as normal by ordinary criteria. Twenty showed less fall, varying from no change at all to more or less greater change, but remaining abnormal throughout.

Patients whose blood pressure fell to normal in sleep had less evidence of disease, less disability and less elevation of blood pressure. Patients who maintained an elevated blood pressure in sleep showed more signs of disease, had more disability and more elevation of blood pressure.

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VENOUS PRESSURE RESPONSES TO EXERCISE IN PATIENTS WITH HEART DISEASE*

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A NUMBER of reports of isolated determinations of venous pressure in various types of cardiac disorder may be found in the literature. Consistent series of determinations in which the venous pressure has been followed from day to day as an index of the progress of the case have been reported by Clark[1] and by Eyster and Middleton.[2] The findings may be briefly stated as those of a high venous pressure with cardiac decompensation, the pressure falling as compensation is reestablished. We have not found any report in which the venous pressure response to exercise has been followed in cases of circulatory disturbance.

One of us[3] has recently reported on the venous pressure response to light or moderate exercise in normal individuals. A general statement concerning the exercise venous pressure curves is that a typical normal response consists of a rise of a few centimeters of water at the onset of exercise followed by a fall coming on after five to ten minutes. The extent of this fall may be such that the venous pressure has returned to its control or resting level while the exercise is still in progress. On cessation of exercise the pressure drops immediately to the resting level; if it has already reached the resting level before the exercise stops there is usually a slight further drop to a subcontrol level. Subsequent work has shown that on heavy exercise normal individuals show a rise of venous pressure which may or may not be followed by the secondary fall. It appears that the closer one is to the limit of his working capacity the less is the possibility of the venous pressure's falling during the progress of the exercise. In every case, however, the pressure in normal individuals drops to or below the control level immediately on cessation of exercise. These results have been interpreted as evidence of a diminution in diastolic heart tone coming on during the exercise. The argument supporting this interpretation has been advanced in previous publications[3, 4] and will not be repeated here.

The work reported here is an investigation of the exercise venous pressure curves on a few cases of various types of cardiac involvement. It seemed probable that patients with clinical manifestations of heart disease would show a curve different from that of a normal individual on the same amount and rate of exercise. The normal subject fails

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to show, or at least shows to a less extent, the secondary fall in pressure when the rate of work approaches his maximum. It might be expected that subjects with heart disease, having a decreased capacity for work, would fail to show the secondary fall of venous pressure at a lower rate of work than would a normal subject. A "normal" curve, as referred to in this paper, is defined as one showing a secondary fall during exercise. It has been established[3] that subjects with clinically normal hearts exhibit a "normal" curve on moderate exercise, about

TABLE I

RESPONSE TO EXERCISE OF VENOUS PRESSURE (IN CENTIMETERS OF WATER)

	Case	C. B.	C. B.	N. F.	S. G.	S. M.	W. M.	A. S.
RESTING CONTROL		11	10	16.5	12.5	14	21	9.5
		11	10	17.5	13	14	21	9.5
		11	10.5	17	12.5	13	21	9.5
				17	12.5	14	21	
					13			
	Min.				12.5			
EXERCISE	1	12	14	18	13	14		9
	2			19.5	14	13		9.5
	3	12	14	21	15	13		8.5
	4			22	15	13		8.5
	5	11	15	21		13		9
	6			20.5		13		9
	7	12	16.5	21		13		9
	8			22		13		9.5
	9	11.5	14	24		12		8.5
	10			25		11		8
	11	11	14	25.5		11		8
	12					11		8
	13	10	13			11		8
	14					11		8
	15	10	12			11		8
	16							
	17	9.5	12					
	18							
	19	10	12					
RESTING AFTER EXERCISE	1	9.5	10.5	25	15	9.5	28	7
	2			23.5	15	9		7
	3	9	11	23	14.5	9	27	8
	4			23	14.5	9		9
	5	9	11	21	14	10	22	8.5
	6			20.5	14	11		9
	7	9	10	19.5	13.5	11	22	9.5
	8			20	13.5	11		9
	9	9	10.5	18.5	13.5	11	22	9
	10			19.5	13	10		9
	11	9	11	19		11	21	9.5
	12			19		10.5		9
	13	10	11	18.5		11	22	9
	14	9.5		18.5		11		9
	15	9.5	11	18.5		11	21	9
	16	10						
	17		10.5					
	18	9.5						
	19		10.5					
	20	9.5						

Vein too small for reading during exercise

C. B. submitted to two observations, doing more work during the second. S. G. stopped after four minutes of exercise because of exhaustion.

300-400 kilogram meters per minute. In the present work we have followed the venous pressure curves of cardiac cases at rates of work even lower than this. In a word it may be said that patients with obviously affected hearts exhibit at very low rates of work (150-250 kilogram meters per minute) the venous pressure response which is seen in normal individuals only as the limit of their working capacity is approached (around 1000 kilogram meters per minute).

The determinations were made on patients working in a chair ergometer. Venous pressure readings were made by a modification[5] of Hooker's[6] apparatus. Respiratory rate, pulse rate and arterial pressure were also followed. The arterial pressure readings were made simultaneously by the Erlanger instrument and by the auscultatory method, the auscultatory systolic and diastolic criteria being electrically signalled on the same drum on which the graphic record was made. The two methods gave closely concordant figures. After the control readings the subject began to exercise, lifting weights on a pulley system by alternate flexion and extension of the lower extremities. The exercise usually continued for fifteen minutes, the readings being made every minute during the exercise and for fifteen minutes after its cessation. The venous pressure data are seen in Table I.

CASE REPORTS

CASE 1.—C. B., Male, aged fifty-one, letter carrier. The present illness began suddenly two months previously with pain under the lower part of the sternum and in the epigastrium. Breathlessness on exertion and weakness and a slow pulse were soon noted. The physical findings included an enlarged heart, dullness extending 11.5 cm. to the left, a systolic murmur at the apex, and a heart rate of 40. The blood pressure was 170 mm. systolic and 65 diastolic. There was moderate sclerosis of the peripheral arteries. The abdomen and lungs were negative and there was no edema. The blood Wassermann was negative. The urine showed a high specific gravity and occasionally albumin, casts, and red cells. The electrocardiogram showed complete A-V heart-block.

Diagnosis.—Chronic myocarditis, complete A-V heart-block, general arteriosclerosis, and hypertension.

CASE 2.—N. F., Male, aged twenty-three, waiter. The past history revealed no etiology for the present illness. For the past six months there had been breathlessness on exertion and for four months palpitation and edema of the legs. The physical examination revealed rather poor nutrition, ragged tonsils, and normal lung signs. The heart was enlarged, dullness extending 11 cm. to the left, with a diffuse precordial pulsation, and at the mitral area systolic and diastolic murmurs and a diastolic thrill. The rhythm was that of auricular fibrillation. The liver was enlarged to 7 cm. below the costal margin. There was ascites, but no edema. The blood Wassermann was negative. The urine showed a trace of albumin and a high specific gravity.

Diagnosis.—Mitral stenosis and regurgitation, chronic myocarditis, auricular fibrillation, chronic passive congestion of the liver and kidneys, and ascites.

CASE 3.—S. G., Female, aged forty, housekeeper. The past history included rheumatic fever at twelve and twenty-five, and chorea at twelve years. For the

last nine years there have been dyspnea and some cough. Hemoptysis occurred nine years ago. There have been also palpitation, weakness, and occasional edema. The physical findings were dyspnea and cyanosis, and enlarged heart, and râles throughout both lungs. The cardiac dullness extended 14 cm. to the left, and there were systolic and presystolic murmurs, a loud first sound, and a presystolic thrill at the apex. The rhythm was regular, the rate 80, the blood pressure 114 mm. systolic and 76 diastolic. The liver was not enlarged and there was no edema. The blood Wassermann was negative.

Diagnosis.—Mitral stenosis and regurgitation, chronic myocarditis, and chronic passive congestion of the lungs.

CASE 4.—S. M., Male, aged fifty-three, meat cutter. The history was merely of pain in the left chest and breathlessness of two months' duration. The physical examination revealed an effusion into the left pleural cavity, moderate sclerosis of the peripheral arteries, a moderately enlarged heart and a blood pressure of 210 mm. systolic and 115 diastolic. The urine contained numerous casts, a few white cells and red cells, and a large amount of albumin, with a low specific gravity.

Diagnosis.—Chronic diffuse nephritis, hypertension, general arteriosclerosis and myocarditis.

CASE 5.—W. M., Male, aged thirty-seven, foreman. The patient had diphtheria at nine years and "chancroid" at eighteen. For the last two years he has had dyspnea and cough, and at times orthopnea. There have been present also weakness and palpitation, and at times pain under the right costal margin and edema of the legs. Physical examination showed slight cyanosis, irregular pupils, râles throughout both lungs, and an enlarged heart, dullness extending 11.5 cm. to the left. There were aortic systolic and diastolic murmurs, a Corrigan pulse, and a blood pressure of 170 mm. systolic and 40 diastolic. The rhythm was regular, the rate 76. The liver extended 5 cm. below the costal margin. There was no edema. The blood Wassermann was positive and the urine contained albumin and casts.

Diagnosis.—Aortic regurgitation, chronic myocarditis, dilatation of the arch of the aorta, and syphilis.

CASE 6.—A. S., Colored Male, aged twenty-four, laborer. The history revealed swelling and pain in the knees and wrists at 12, lasting two years. The eyes became "yellow" at twelve. Ulcers developed on the legs at sixteen and have persisted. Breathlessness on exertion has been present for three years, and swelling of the ankles for one year. Weakness had been present for several weeks. Physical examination showed fair nutrition, pallor of the nail beds and greenish sclerae. The cardiac dullness extended 12.5 cm. to the left and there were systolic murmurs at the apex and pulmonic area. The lungs and abdomen were negative. There were ulcers of both legs, but no edema. The blood contained 2,000,000 red cells, 12,000 white cells per cubic mm., 55 per cent hemoglobin, and many sickle-shaped red cells. The blood Wassermann was negative. The urine contained albumin. The electrocardiogram showed a P-R interval of 0.21 sec.

Diagnosis.—Sickle cell anemia, hypertrophy of the heart, chronic myocarditis, and ulcers of the legs.

To conserve space only the venous pressure data are given. The subjects may be identified by their initials for reference to the case reports. It will be noted that subjects with obvious cardiac decompensation show a high resting venous pressure which rises considerably on exercise, the rise being maintained throughout the exercise. Furthermore, the return to normal on cessation of exercise is

not immediate, as with normal subjects. Venous pressure readings were not possible on W.M. during exercise, because of the great decrease in caliber of the vein. That the pressure was raised is shown by the fact that the readings in the post-exercise period are still considerably above the control level. A general statement, to which there are certain exceptions, of the behavior of the arterial pressure, is that the systolic is increased on exercise, the diastolic to a less extent, the pulse pressure being increased. After exercise the systolic pressure falls, the resting level usually being reached in one minute in the subjects with the best compensation. The fall to the resting level is prolonged over two to five minutes in the poorly compensated cases. The diastolic pressure returns to the resting level on the first reading in the post-exercise period even in those cases where the return of the systolic is delayed. The pulse rate, except in the case of C.B. (complete heart block), is increased on exercise, the extent of the increase varying with the rate of exercise and the condition of the patient. The same may be said of the respiratory rate. The pulse rate, even in the decompensated cases, returns to normal within three minutes after exercise.

At the beginning of this work it was our hope that the departure from the normal of the venous pressure response to exercise might be a relatively early manifestation of myocardial involvement. If this were the case, the venous pressure curve might be an objective diagnostic and prognostic index in early or mild cases. We have found, however, that a departure from the normal curve on light exercise is seen only in cases where the cardiac involvement is obvious; it does not detect slight degrees of involvement. The procedure will serve as a rough index of the extent of cardiac insufficiency by determining the maximum rate of work at which the "normal" venous pressure curve is obtained; the less efficient the heart, the lower the rate of work at which the secondary fall of venous pressure fails to appear.

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THE COMPARATIVE RATE OF ABSORPTION OF FRESH AND OF OLD TINCTURES OF DIGITALIS*

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USING the usual frog methods for assay, investigators unanimously agree that tincture of digitalis loses strength with the passage of time. On the contrary, repeated assays on the part of ourselves and others by the cat method, in which the drug is introduced intravenously, have given indications that deterioration of highly alcoholic preparations of digitalis occurs to only a slight extent. This suggests the possibility that what is interpreted as deterioration merely represents a change in the tincture which interferes with its absorption from the lymph sac of the frog.

The difference in the results obtained by the two methods of assay at the time of percolation and five years later is illustrated in Table I. Our tincture No. 36 was percolated in the winter of 1916 from digitalis grown in Virginia and was assayed within three months by both the cat method and the official frog method. In the spring of 1922, a little over five years after the initial assays, the tests were repeated. These comparative assays show a marked loss in strength by the frog method, while the apparent deterioration, as determined by the cat method, is well within the limit of error.

TABLE I

TINCTURE DIGITALIS NO. 36

Initial and subsequent potency by different assay methods

	1917 ASSAY MG. X KG.	1922 ASSAY MG. X KG.	PER CENT LOSS
Frog method	0.15	0.35	57%
Cat method	42.20	43.10	2%

Assuming that the change in the tincture actually involves its absorbability from the frog's lymph sac, the question arises whether absorption from the alimentary tract of man is not similarly affected. Though it has been assumed by Paranjpe[1] that absorption from the lymph sac of the frog parallels absorption from the human intestine, this has never been proved. In fact, some experimental evidence was brought forward by Hatcher and Eggleston[2] which supports the opposite view. Ouabain, for example, is rapidly absorbed from the lymph

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sac, but is poorly absorbed from the intestines, while exactly the opposite is stated to be the case with digitoxin.

In order to determine the relative absorbability of old and fresh tinctures, a comparison was first made on cats. In these experiments the procedure suggested by Hatcher was employed. The cats were

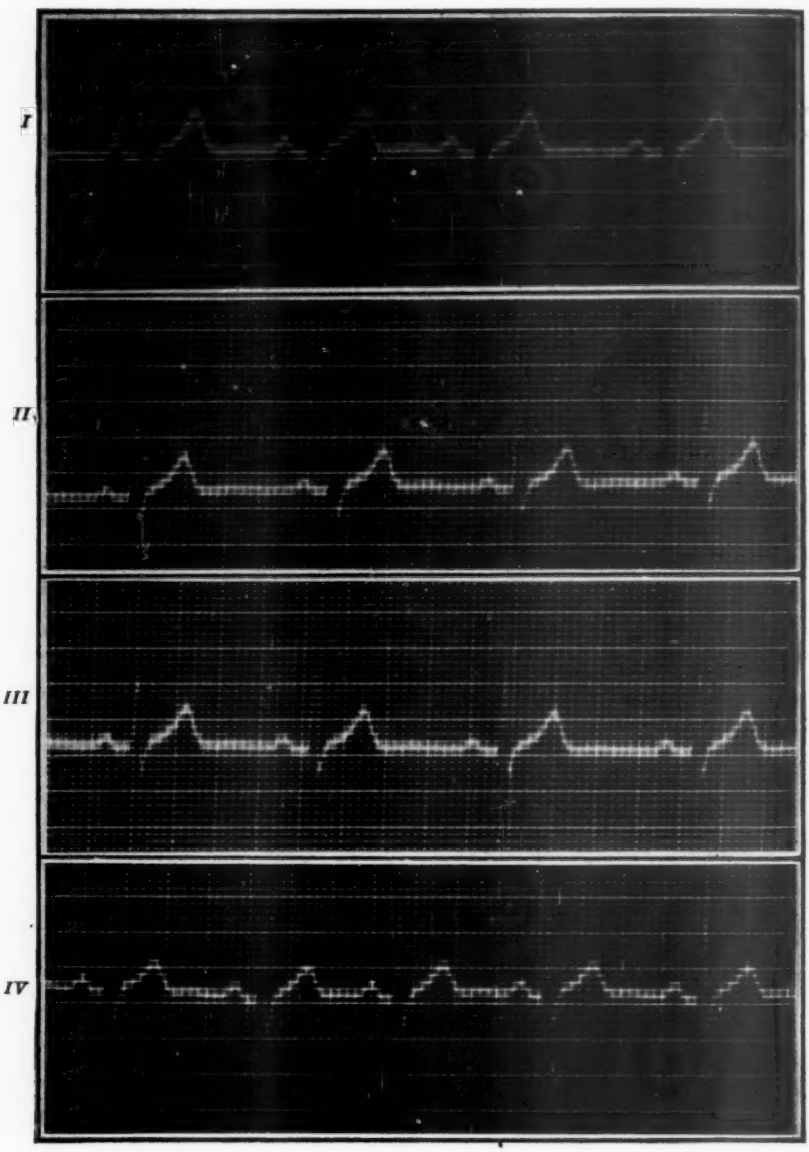

Fig. 1.—Case 1. Change in T-wave, Lead II, after a single dose of digitalis. Fresh tincture S-2.

I. Before digitalis, T-wave 5.1 mm. *II.* One hour after dose. T-wave 4.5 mm. *III.* Two hours after dose. T-wave 4.4 mm. *IV.* Six hours after dose. T-wave 3.4 mm.

Total change in height of T-wave in six hours 1.7 mm., a drop of 33 per cent.

fasted for twenty-four hours and then were given by mouth 1 c.c. of the tincture per kilogram body weight diluted with nine parts of water. In exactly one hour the cats received an intraperitoneal injection of chloretone, 0.2 gm. per kilogram of body weight. Shortly after this the animals were arranged for receiving intravenous injections of 1:100,000 ouabain solution. These injections were started exactly two hours after administration of the tincture and the rate of injection was 1 c.c. every two minutes until death occurred. The average fatal dose of ouabain is 0.1 mg. per kilogram of body weight, equivalent to 10 c.c. of the 1:100,000 solution. Obviously, the difference between this theoretical fatal dose and the dose of ouabain solution actually required to cause death represents the amount of tincture already absorbed, since ouabain and digitalis are truly synergistic in their lethal action on the cat.

These experiments on the comparative absorbability of digitalis from the alimentary tract of cats were done in 1922 and we used our tincture No. 36, which at that time was five years old, and compared it with two freshly percolated tinctures. Tincture No. 36 was very potent with a cat unit of 41.05 mg. In Table II is shown the comparison with a fresh tincture, S-1, which was also very potent with a cat unit of 38.44 mg.

TABLE II

ABSORPTION OF DIGITALIS FROM THE ALIMENTARY TRACT OF CATS

Comparison of a 5-year-old tincture with a fresh tincture of approximately equal potency

TINCTURE USED	CAT UNIT	NUMBER OF CATS USED	AMOUNT ABSORBED IN 2 HOURS	PER CENT OF LETHAL DOSE ABSORBED IN 2 HOURS
Fresh Tr. S-1	38.44	10	11.5 mg. x kg.	30.0%
Old Tr. 36	41.05	23	8.9 mg. x kg.	21.7%

From the results shown in Table II it is apparent that the absorption of digitalis from the alimentary tract of cats is definitely less in the case of the old tincture when compared with a fresh tincture of approximately equal potency, as determined by the cat (intravenous) method of assay.

Comparison of the absorption of old and fresh tinctures of digitalis from the lymph sac of the frog with the amount of absorption from the intestine of cats is indicated in Table III. The figures in this table show that there is a definite lessening of absorbability in the case of the five-year-old tincture from both the lymph sac of the frog and from the alimentary tract of the cat. Furthermore, the degree of loss of absorbability of the old tincture is practically identical in the case of the lymph sac of the frog and the intestine of the cat.

Finally, it remains to be determined whether, with the lapse of time, a change takes place in tincture of digitalis which interferes with absorption from the human alimentary tract. It is very probable that

TABLE III

ABSORPTION OF DIGITALIS FROM THE LYMPH SAC OF THE FROG AND FROM THE ALIMENTARY TRACT OF THE CAT

Comparison of a five-year-old tincture with a fresh tincture of approximately equal cat unit strength

TINCTURE USED	CAT ASSAY	CAT RATIO	FROG ASSAY	FROG RATIO	ABSORPTION ASSAY 2 HOURS	ABSORPTION RATIO
Fresh Tr. S-1	38.44	100	0.25	100	30% of L.D.	100
Old Tr. 36	41.05	94	0.35	71	21.7% of L.D.	72

intestinal absorption in the cat and in man is parallel. This has not been heretofore demonstrated but our results would tend to prove it.

In the clinical experiments, of course, the scheme of dosage is different. In our tests on human individuals the tincture was given in a single dose in the morning on a fasting stomach. Just preceding this an electrocardiogram was taken to serve as a normal control, and further electrocardiograms were taken at varying intervals up to six hours after the dose was administered. The subjects were healthy medical students and young assistants. In order to facilitate measurement of the T-wave the galvanometer string was standardized to a deflection of 1.5 cm. per millivolt instead of the customary 1 centimeter.

The experiments of Cohn, Fraser and Jamieson,[3] of White and Sattler,[4] and of Pardee,[5] have shown the significance of lowering, or inversion, of the T-wave of the electrocardiogram as an early sign of the action of digitalis on the human heart. A single dose of ½ minim of the tincture per pound of body weight will cause a definite flattening or lowering of the T-wave which can be observed in from two to four hours and reaches its maximum in six or seven hours.

In our experiments to compare the absorbability of old and fresh tinctures of digitalis from the human alimentary tract, ten subjects were used. In order to insure complete elimination of the previous dose, the second tincture was given four weeks after the first one. Figs. 1, 2 and 3 illustrate the type of experiment and demonstrate

TABLE IV

HEIGHT OF T-WAVE IN MILLIMETERS, IN LEAD II OF ELECTROCARDIOGRAM, FOLLOWING THE ORAL ADMINISTRATION TO HUMAN BEINGS OF A SINGLE DOSE OF A NINE-YEAR-OLD TINCTURE OF DIGITALIS, O, AND OF A FRESH TINCTURE, F

Subject	1		2		3		4		5		Average	
Tincture used	O	F	O	F	O	F	O	F	O	F	O	F
Before digitalis	4.2	5.1	4.2	4.0	5.4	4.1	5.5	5.4	3.3	2.0	4.52	4.12
1 hr after dose	3.9	4.5	...	3.8	5.4	4.0	...	...	3.3	2.0	....	....
2 hrs after dose	3.8	4.4	3.3	3.6	5.2	4.0	5.2	4.3	3.2	1.9	4.14	3.64
6 hrs after dose	3.3	3.4	2.8	2.6	3.4	2.8	4.6	3.9	2.6	1.4	3.34	2.82
Total drop 6 hrs	0.9	1.7	1.4	1.4	2.0	1.3	0.9	1.5	0.7	0.6	1.18	1.30
Percentage drop	21	33	33	35	36	32	16	28	21	30	26.1	31.6

Old tincture No. 36; dose 0.045 cat unit per pound body weight.
Fresh tincture No. S-2; dose 0.041 cat unit per pound body weight.
Galvanometer string standardized: 1.5 cm. to 1 millivolt.

graphically the lowering of the T-wave after a single dose of digitalis. An effort was made to standardize the galvanometer string exactly to 1.5 cm. deflection per millivolt, but in any case in which the tension of the string was not accurately adjusted an allowance was made in calculating the height of the T-wave. Overshooting was not encountered,

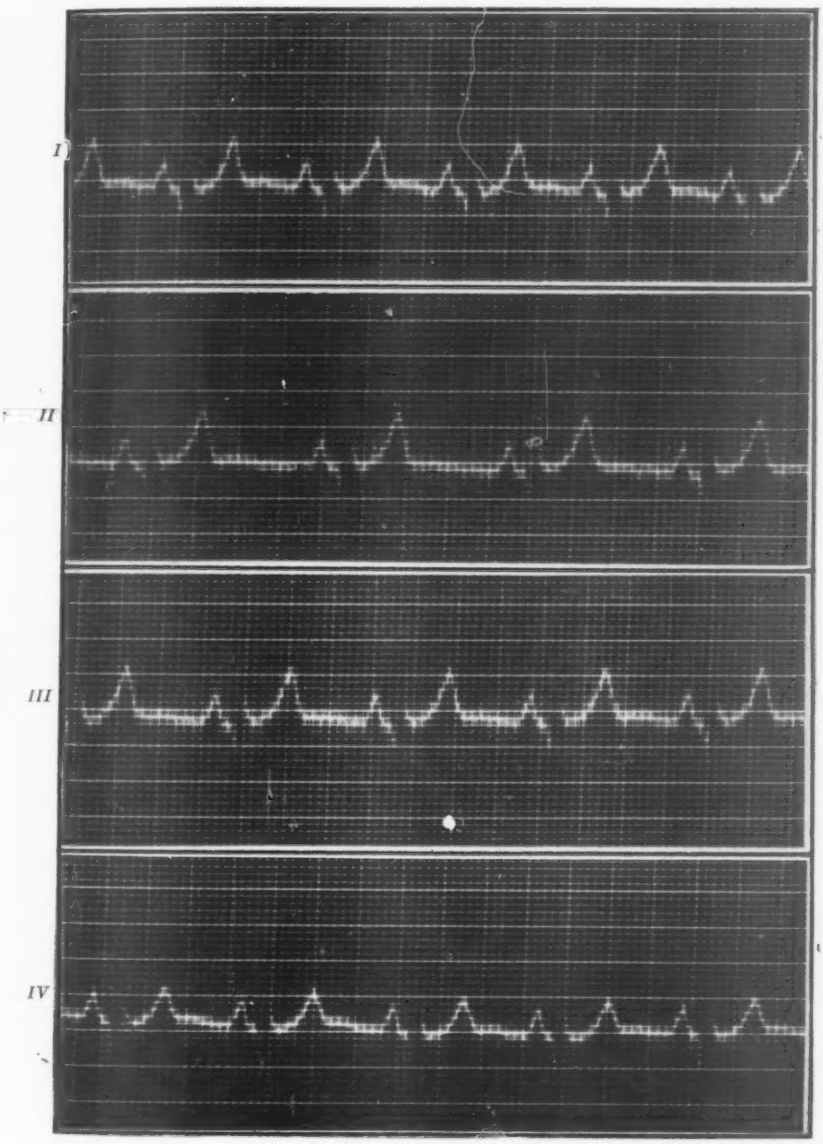

Fig. 2.—Case 3. Change in T-wave, Lead II after a single dose of digitalis. Old tincture 36.

I. Before digitalis. T-wave 5.4 mm. *II.* One hour after dose. T-wave 5.4 mm. *III.* Two hours after dose, T-wave 5.2 mm. *IV.* Six hours after dose, T-wave 3.4 mm.

Total change in height of T-wave in six hours 2.0 mm., a drop of 36 per cent.

due to the fact that the laboratory was well heated and the electrodes were wrung out in warm saline just before being applied.

Table IV gives the results of the effect on the T-wave in five subjects after the ingestion of a single dose of a nine-year-old tincture compared with an equal dose of a fresh tincture. In the case of the old tincture No. 36, with a cat unit of 41.05 mg., $\frac{3}{10}$ of a minim per pound body weight was given, equivalent to 0.045 cat unit per pound.

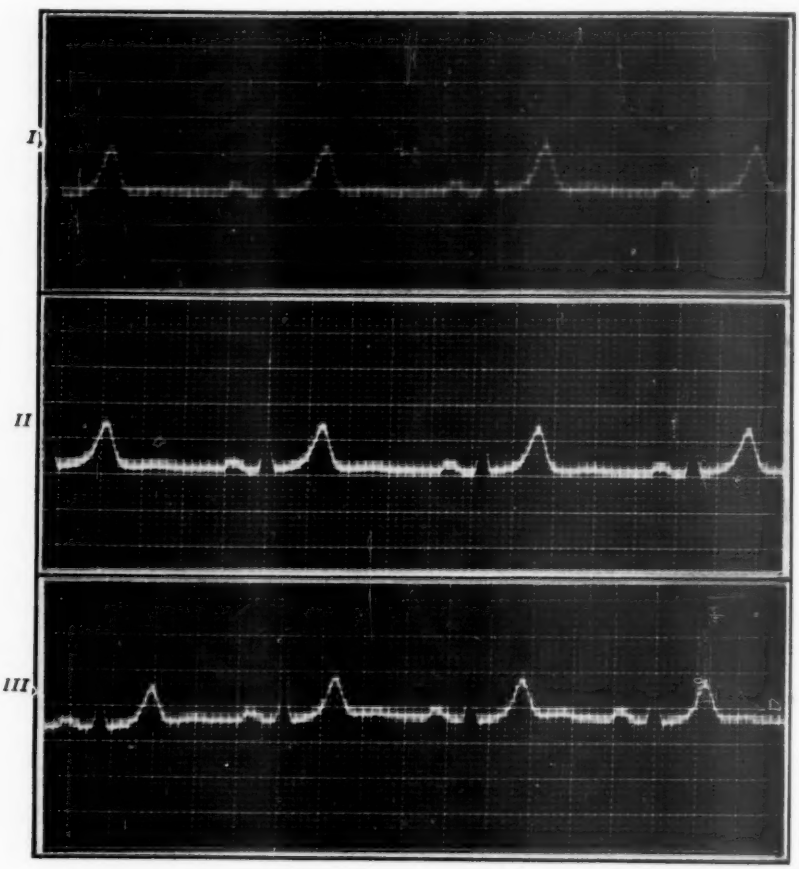

Fig. 3.—Case 4. Change in T-wave, Lead II, after a single dose of digitalis. Old tincture 36.

I. Before digitalis, T-wave 5.5 mm. *II.* Two hours after dose, T-wave 5.2 mm. *III.* Six hours after dose, T-wave 4.6 mm.

Total change in height of T-wave in six hours, 0.9 mm., a drop of 16 per cent.

Of the fresh tincture, No. S-2, with a cat unit of 75.60 mg., ½ minim per pound body weight was administered, equivalent to 0.041 cat unit per pound.

Analysis of the results in Table IV shows, in the case of the old tincture, an average lowering of the T-wave in the five subjects of

26.1 per cent in six hours. With the fresh tincture the average lowering of the T-wave in the five subjects was 31.6 per cent in six hours.

Table V shows the lowering of the T-wave in five other subjects following the ingestion of a single dose of the fresh tincture (No. S-2, cat unit 75.6 mg.) compared with another nine-year-old tincture (No. 32, cat unit 76.0 mg.). The dose with each tincture was ½ minim per pound body weight equivalent to 0.041 cat unit per pound. The average lowering of the T-wave with this old tincture in the five subjects was 24.6 per cent in six hours compared with a lowering of 33.7 per cent in the case of the fresh tincture.

TABLE V

HEIGHT OF T-WAVE IN MILLIMETERS, IN LEAD II OF ELECTROCARDIOGRAM, FOLLOWING THE ORAL ADMINISTRATION TO HUMAN BEINGS OF A SINGLE DOSE OF A NINE-YEAR-OLD TINCTURE OF DIGITALIS, O, AND OF A FRESH TINCTURE, F

Subject	6		7		8		9		10		Average	
Tincture used	O	F	O	F	O	F	O	F	O	F	O	F
Before digitalis	5.2	5.4	4.7	6.7	5.8	5.3	5.7	5.1	3.8	4.8	5.04	5.46
2 hours after dose	4.9	5.4	4.5	6.1	5.8	5.1	5.6	...	3.7	4.6	--	--
6 hours after dose	3.9	4.7	2.6	4.2	5.1	4.5	4.6	2.3	2.8	2.4	3.80	3.62
Total drop 6 hours	1.3	0.7	2.1	2.5	0.7	0.8	1.1	2.8	1.0	2.4	1.24	1.84
Percentage drop	25	13	45	37	12	15	20	55	26	50	24.6	33.7

Old tincture No. 32; dose 0.041 cat unit per pound body weight.
Fresh tincture No. S-2; dose 0.041 cat unit per pound body weight.
Galvanometer string standardized: 1.5 cm. to 1 millivolt.

Combining the results on the ten subjects in Tables IV and V gives an absorption ratio of the fresh tincture compared with the old tinctures of 100 to 77. Reference to Table III shows that this absorption ratio from the human alimentary tract agrees very closely with the absorption ratio from the lymph sac of the frog and from the alimentary tract of the cat. At the same time these three absorption methods of assay—frog, cat and human being—while agreeing very closely with each other, do not accord with the intravenous cat method of assay.

As the result of these experiments, it would be inferred that the intravenous cat method of assay would be the procedure of choice in those rather exceptional instances in which digitalis is to be therapeutically administered by vein. On the other hand, when digitalis is to be given by mouth, assay by the official frog method would appear to give a more exact idea of the potency of the preparation.

CONCLUSIONS

Our deductions are, therefore, that tincture of digitalis does not "deteriorate" with age when it is tested and employed intravenously, but that a definite "loss of absorbability" occurs with the passage of time and that this change interferes to an almost equal extent with

absorption from the lymph sac of the frog, from the alimentary tract of the cat and from the alimentary tract of man.

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THE INDEPENDENCE OF ELECTRICAL AND MECHANICAL REACTIONS IN THE MAMMALIAN HEART*

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ARGUMENT

THE conception that the initial electrical deflections related to the onset of ventricular systole are due to the progressive spread of the impulse rather than to the contraction process itself, has been gaining steady experimental support within recent years (for a recent review, cf. Arbeiter[1]).

As far as cardiac tissue is concerned, the nature of the evidence consists briefly; (1) in the precedence of the electrical over the mechanical changes, and (2) in the lack of correspondence between the amplitudes of the electrical and mechanical variations, including the observations that distinct electrical changes may occur when the heart is quiescent. Within recent years, however, this conception has received a decided check by the careful observations of Einthoven and his associates,[3, 4, 5, 9] which indicate that such results may be attributed partly to technical errors in the manner of leading adopted, but largely to the fact that the sensitivity of apparatus utilized to record mechanical changes has in no wise equaled that employed to record electrical variations.

In 1915, Garten[6] had shown that the intraventricular pressure recorded by his electrically recording manometer began to rise only .017 to .021 sec. after the beginning of R_{II} of the electrocardiogram. Unaware of the work of Garten, owing to the fact that German periodicals were not available during the World War, I had undertaken similar experiments, utilizing optical manometers of my own design. The results which were alluded to briefly in 1917,[15] but never published in detail in view of Garten's prior communications, indicated that the intraventricular pressure rose .03 to .045 sec. after the initial rise of R_{II}, thus placing the onset of ventricular contraction on the descending limb of R_{II}. Applying the axiom that "obviously no dynamic process can be held responsible for any electrical variation with which it is not isochronous," the conclusion was reached that the QRS deflections of the electrocardiogram are not associated with the contraction process but rather with the propagation of the impulse over the ventricular muscle.

Two subsequent experiences have, however, invalidated the conclusiveness of this deduction. Examination of records subsequently

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obtained showed considerable variation in the time relations, with an occasional value of about .01 sec. An idea of the range of variations may be obtained by consulting Table I of this article which gives values for experiments reported upon at this time, under the heading ECG. The recent observations of Katz[8] that the right and left ventricles do not begin their contractions synchronously, offer a possible clue to the explanation for such time differences; on the other hand, they also make it doubtful whether comparisons of the electrical deflections largely due to right ventricular activity with mechanical activity of the left ventricle are quite conclusive in deciding the question as to the isochronicity of electrical and mechanical changes in either ventricle.

For this reason, it seemed desirable to study the relation between the development of negativity over various surface areas of the two ventricles and the pressure variations within the ventricles. These comparisons were selected on the assumption that by the time intrinsic negativity appears over the surface of either ventricle, the whole septum as well as the entire thickness of the ventricular wall at that point must have been excited; consequently *if electrical variations are an accompaniment of the contraction process,* surface negativity should never precede but follow, by reasonable intervals, the rise of pressure within the ventricle in question.

Obviously, however, such comparisons may only be regarded as crucial provided we are further assured; (1) that the optical manometers record the first elevation of intraventricular pressure without lag; (2) that the earliest contraction of comparatively small blocks of muscle tissue is capable of elevating intraventricular tension; and (3) that our method of lead really records surface negativity.

Qualifications of the Optical Manometers.—The criticism of Einthoven and his associates[3, 4, 5, 9] that the apparatus used for recording mechanical contractions is not sensitive enough to be used in comparison with electrical records, does not apply to the optical apparatus used for recording intraventricular pressures. In these experiments the universal optical manometer described by Baker and the writer[19] was employed. When covered by rubber dam 0.85 mm. in thickness, tightly stretched over the segment capsule, the manometer had a vibration frequency of 167 per sec. and recorded a curve 53 mm. in amplitude for 100 mm. variation in pressure. In special experiments, the rubber was stretched less so that the sensitivity was greatly increased, of course at the expense of vibration frequency, which never fell below 113 per sec., however. It is obvious that such apparatus can be depended upon to respond without lag to pressure variations which are less than 1 mm.

The Relation of the Rise of Intraventricular Pressure to the Inception of Ventricular Contraction.—In a comparatively recent discussion

with Prof. Einthoven as to the time relations of the initial deflections of the electrocardiogram and the rise of intraventricular pressure, he justly raised the question as to how far the ventricular contraction process must have advanced before sufficient energy is developed to cause an increase of intraventricular pressure, measurable even by sensitive manometers. Practically, this question may be fractioned into the following: (1) How large a bulk of contracting muscle is required to initiate an elevation of tension? and (2) Are the initially contracting muscle fibers so arranged that the contractile force exerted by them causes an elevation of intraventricular tension?

Fortunately, there are experimental data which favor the view that only a small contractile force is required to elevate the pressure within the ventricle, and there are both experimental and anatomical arguments that support the belief that the first contraction processes in the ventricle occasion a prompt elevation of tension.

Some idea as to the contracting muscular mass required to elevate intraventricular tension under natural conditions may be gleaned from the effects of auricular contraction. While auricular contraction under good circulatory conditions as a rule causes but a small elevation of intraventricular pressure (cf. Figs. 4 and 5) the change is distinctly recognizable and, what is more important still, begins before the summit of the intraauricular wave has been reached in the auricle (cf. Wiggers[16]). In view of the fractionate nature of auricular contraction (Wiggers,[17] Lewis, Feil and Stroud[11]) this means that a contractile force equivalent to that developed by only a small part of the thin auricular musculature is capable of causing a discernible variation of pressure, when applied to the ventricular contents.

Probably the most reliable evidence as to the very onset of muscular contraction in the ventricles is given by the beginning of the sound vibrations which they set up. The main vibrations characteristic of the first sound, however, begin precisely with the elevation of intraventricular pressure, thus furnishing probable evidence that the rise is coincident with the very beginning of muscular contraction. It is true that *"introductory vibrations"* have been described by Battaerd[2] which precede both the main vibrations (Battaerd,[2] Hess[7]) and the rise of intraventricular pressure (Wiggers and Dean[20]) by .035 to .06 sec. Such vibrations are sometimes assigned to contraction of the papillary muscles, or are cited as evidence that ventricular contraction does occur before it is capable of detection by other means (Einthoven[3]). There is no experimental proof, however, for such assumptions; indeed, many facts are opposed to such an interpretation. In the first place, the periods of these vibrations are so long, the amplitude so small and their very presence so variable—even in sounds recorded directly from the heart as was done by Wiggers and Dean[20]—that it is highly questionable whether they are actually a

part of the first heart sound. The entire periods of systole and diastole not occupied by vibrations of the regular sounds are filled with various sorts of vibrations which are probably due to changes in the flow of blood into and out of the ventricle. Therefore, these small introductory vibrations may easily result from causes other than muscular contraction. In the second place, a careful study of their time relations makes it difficult to conceive of their being due to muscular contraction. Frequently they begin .05 to .065 sec. before the main vibration of the first sound (Battaerd[2], Hess[7]) or the rise of intraventricular pressure (Wiggers and Dean[20]) thus placing them during the early phase of auricular relaxation as actually demonstrated by auricular myograms (Wiggers and Dean[20]). Time comparisons of dynamic and electrical changes such as have been presented in diagrammatic form by the writer[15] indicate that at this moment the wave of negativity has not yet reached the ventricle.

We may now analyze the question as to whether the initially contracting fibers are so arranged that their contractile force can at once be exerted on the ventricular contents. Owing to experimental difficulties, absolutely crucial data as to the relative time of negativity of the septum, papillary muscles and the endocardial surfaces of the heart are difficult to obtain. The only figures in existence to my knowledge are those of Lewis and Rothschild,[12] and as is recognized by these investigators, they permit deductions which are probable rather than quite final. Nevertheless, the earliest readings obtained are from the septum, which together with the fact that it fits in with many other experimental observations as well as anatomical evidence as to the course of excitation, makes probable the conception that the interventricular septum is initially excited and presumably contracts first. Further, we may be certain that the excitation and contraction of the papillary muscles do not lag far behind. If it be accepted that the muscular septum contracts earliest, we must inquire whether the fibers of this structure are so arranged that the force of contraction developed can be brought to bear upon the fluid within the ventricles and thus elevate the tension promptly. To be all inclusive, we must further explain how it is possible for contraction of a common septum to influence the pressure on one side before the other, as was found to be the case by Katz[8] and was again corroborated in some experiments of this research (cf. Fig. 4).

To begin with, the muscular septum dividing the ventricles is not a single or simple structure but a complex aggregate of bundles or fasciculi arranged in different layers. The chief bulk of the muscular septum is composed of circularly arranged fibers which are a part of the deep bulbospiral system encircling the left ventricle. The lower portion is also the termination of the superficial bulbospiral system which enters into the interior and forms an oblique layer directed

posteroanteriorly and upward. Finally, the entire septum contains many longitudinal fibers among which is the LRV bundle, which passes from the median wall of the right ventricle to the aortic septum (Mall,[13] MacCallum[14]).

A dissection of a dog's heart from the right side, such as is shown in the photograph of Fig. 1, shows the relation of these layers to the right ventricular cavity. The musculature underlying the right

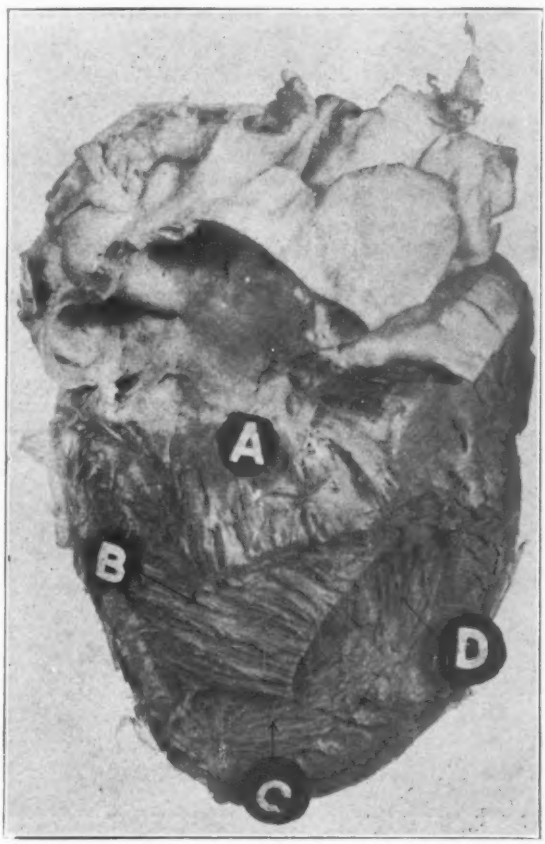

Fig. 1.—Photograph showing layers of interventricular septum, as viewed from right side; *A*, right longitudinal layer; *B-C*, circular and oblique layers; *D*, left longitudinal layer.

bundle branch consists of a rather thick fasciculus of longitudinally directed muscle fibers, shown as the cut muscle *A* in Fig. 1. Beneath this lies a thicker layer of nearly circular muscle fibers marked *B*. Beneath this, in turn and in closer relation to the left ventricular cavity is a thick layer of fibers marked *C*, which are directed obliquely upward and forward. It will be noticed that their direction is almost at right angles to those of the layer *B*. Finally there appears, in the small exposure still permissible, another very thin layer of longitudinal

fibers *(D)* lying just beneath the left bundle branch and its divisions, when dissection is made from the left side.

If, as anatomical and experimental considerations lead us to believe, the external layers of the muscular septum are the first to be excited by twigs of the A-V bundle branches and if the excitation wave passes through the muscle layers of the septum toward the median line, then it becomes obvious that a thick layer of longitudinally directed muscles *(A)* is first excited on the right side while the obliquely but more circu-

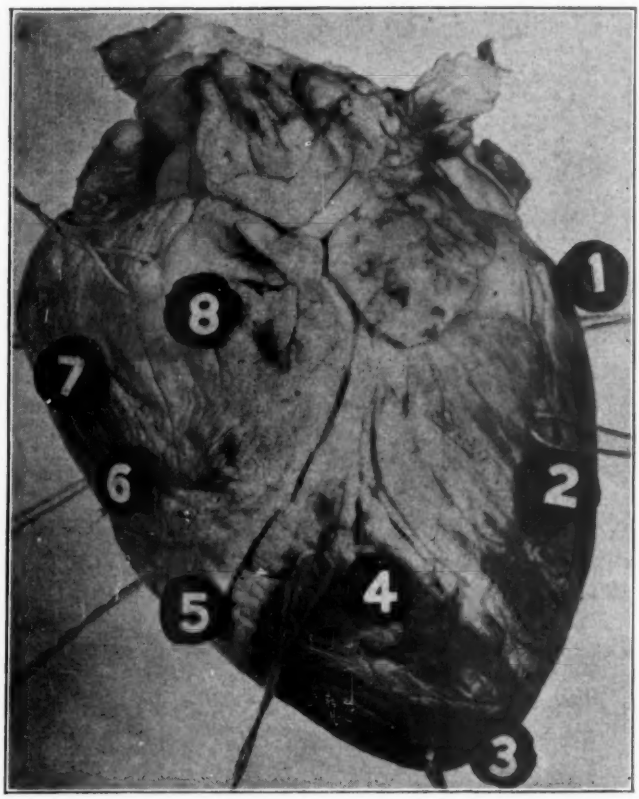

Fig. 2.—Photograph of anterior surface of heart, showing points from which direct leads were taken by threads. Numbers correspond to records in Fig. 4.

larly directed muscles *(D)* are excited much earlier on the left side. The fact that such differently directed bundles are initially excited on the two sides may possibly furnish a morphological explanation as to the reasons why left and right ventricular pressures do not always rise simultaneously and that they change with different degrees of cardiac distention as shown by Katz.[8] For, while there can be little question that the shortening and thickening of circularly disposed fibers must compress the ventricular contents at the moment their contraction starts, we may not be so certain from anatomical considerations

alone, that contraction of the longitudinally directed fibers has a similar immediate effect. Their direction and location would lead us to believe that their shortening serves either to draw the apex upward or the membranous septum and its continuation into the aortic septum downward, while their thickening might be much less effective in elevating intraventricular tension promptly.

Several experimental facts, however, make it improbable that such suspicions based on anatomical considerations are valid. In the first place, if this were true, we should expect a *regular* precedence of

Fig. 3.—Sketch showing extent of areas included in leads incorporated as data of Tables I and II.

the left ventricular pressure rise as is shown, for example, in Fig. 4. The experimental results of Katz[8] show, however, that while in any series of experiments the number of cases with left ventricular precedence predominates, cases in which right ventricular precedence occurs are quite common. Further, during the course of any series of experiments the order of sequence in the same heart may be changed by experimental means. In the second place, if the contraction of longitudinal strands exerted a traction on the membranous interventricular and aortic septum we might anticipate changes in the aortic pressure curves before the elevation of intraventricular pressure occurred. Pre-

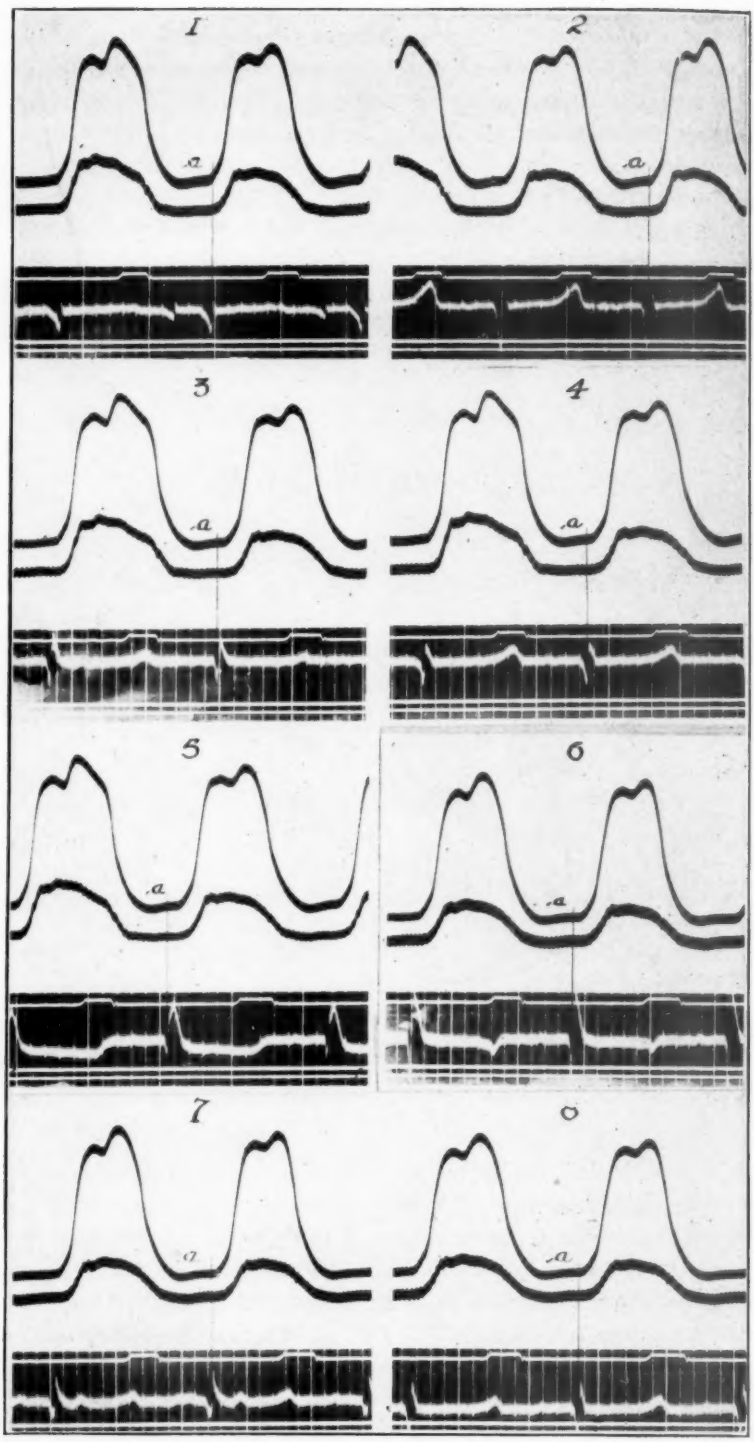

Fig. 4.—Eight segments of records showing left intraventricular pressure (upper), right intraventricular pressure (middle), and electrograms from points corresponding to those shown in Fig. 2. *a*, **Auricular wave; time, 0.04 second, description in text.**

liminary vibrations in the aortic pressure curve previous to the main pressure rise during systolic ejection have been described and analyzed (for references and details cf. Wiggers,[16] page 423) but careful studies have also shown that the earliest variations never precede but often follow the rise of intraventricular pressure. Illustrations of such effects of ventricular contraction on aortic pressures are shown in Figs. 5 and 6. In the former, the vibration *b-c* which can be attributed to a trac-

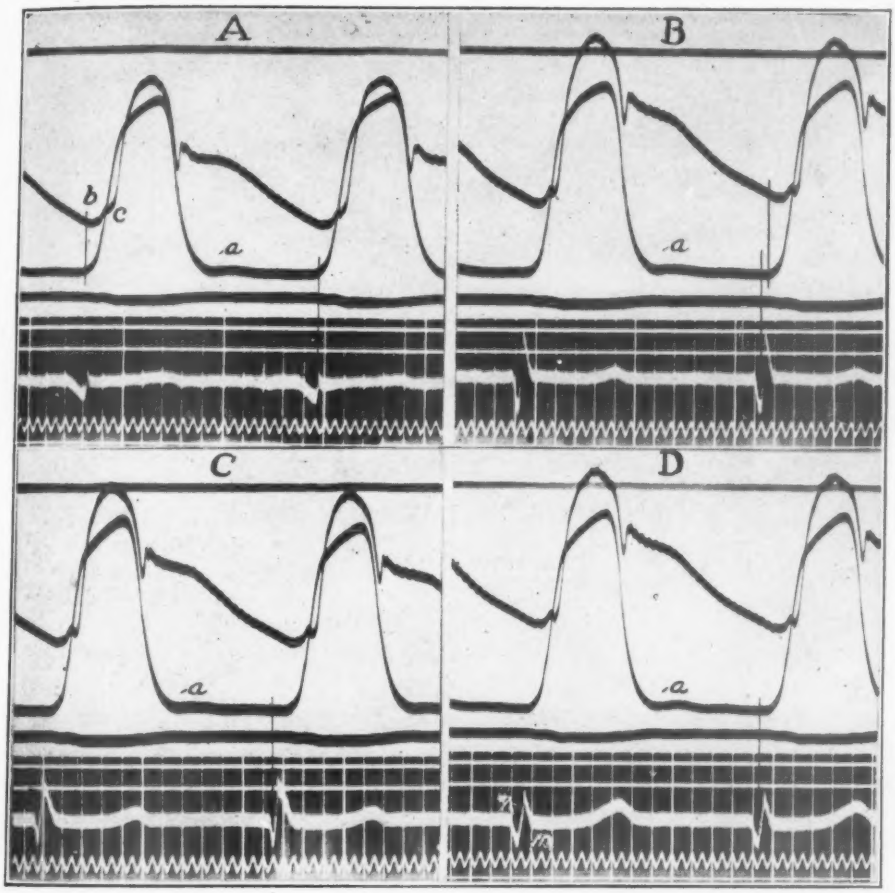

Fig. 5.—Four segments of record showing relation of aortic and left intraventricular pressure curves to electrograms. *A*, point 1; *B*, point 3; *C*, point 5; *D*, point 7; time, 0.04 second; *a*, auricular wave; *b*, *c*, *d*, initial aortic vibrations; *m*, *n*, break in electrical deflections. Discussion in text.

tion effect, begins slightly after the elevation of left intraventricular pressure; and in the latter, the dip *b-c* occurs precisely with the pressure rise. Certainly, as far as left ventricular pressure is concerned, experimental evidence is opposed to the possibility that contraction in longitudinal fibers occurs before the intraventricular pressure rises.

If, however, we fail to concur in the view that contraction starts

first in the interventricular septum, then we must fall back on the papillary muscles as the seat of initial contraction. This must be accompanied by the frank admission that the contraction of such muscular papillae projecting into the cavities of the ventricle may be without effect on intraventricular pressure. If, however, their contraction precedes in this way, they must exert a pull or a tug on the valve leaflets through the chordae tendineae. If this were true we should

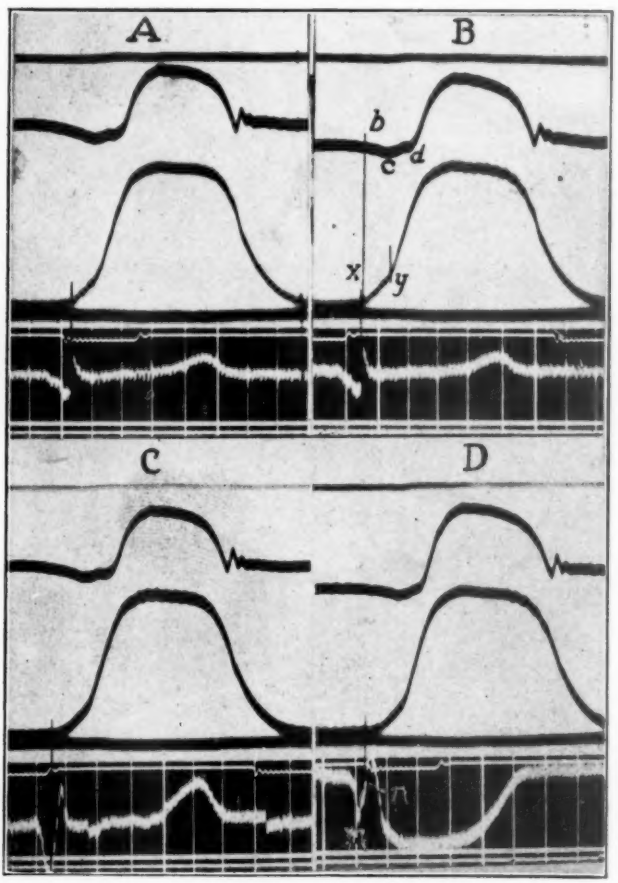

Fig. 6.—Four segments of records showing relation of aortic and left intraventricular pressure curves to electrograms. *A*, point 1; *B*, point 2; *C*, point 3; *D*, point 5; time 0.04 second; *b, c, d,* initial aortic vibrations; *m, n,* break in electrical deflections; *x, y,* initial elevation of intraventricular tension. Discussion in text.

expect them to set up some sort of vibrations capable of affecting the much more sensitive optical manometers commonly employed to record intraauricular pressures. Comparisons of such intraauricular curves with those of intraventricular pressures, however, not only fail to show the occurrence of such wavelets previous to the rise of ventricular pressures, but further show not the slightest deviation from the smooth fall of the auricular wave until the moment when intraven-

tricular pressure rises (Wiggers,[16] Fig. 1). Accurately designed experiments, therefore, give no support to the belief that the papillary muscles contract previous to the elevation of intraventricular pressure.

I have entered into this rather lengthy discussion—perhaps to the point of becoming wearisome—in order to establish in as critical a manner as possible that our anatomical and experimental stock of facts does not support the objection so easily made without supplementary proof, that the initial elevation of intraventricular pressure is not the first index of muscular contraction.

Method of Lead.—In order that unipolar leads from a whole series of points on the two ventricular surfaces could be compared in rapid succession with intraventricular pressures and repeated tests made from the same points, the following technic was found most suitable:

One nonpolarizable indifferent electrode was sewed under the skin of the upper thorax in the median line. Stitches of No. 8 cotton thread previously soaked in strong saline were placed in the heart so that they just pierced the outer layers of cardiac muscle. No evidence exists that the slight injury so caused affects the time of negativity in any way, nor was any injury current detectable in the system on closing the circuit through the galvanometer string. On the other hand, the definite localization of points thus obtained is of major advantage in taking records in rapid succession, or in repeatedly comparing the same points. After the optical manometers had been adjusted and fixed in relation to the camera and projection lamp, a series of nonpolarizable boot-electrodes were placed around the manometers and to these the twisted threads from various points of the heart were securely tied, sufficient slack being left so that no tugs of the heart on the boot-electrodes could occur. These boots were in turn connected to a rotary switch which made it possible to connect in succession each different point on the heart with the string of a Hindle galvanometer, the return lead always being made through the indifferent electrode. During the course of an experiment, the threads required repeated moistening but careful tests showed that drying had no other influence than to modify the amplitude of the recorded electrical variations. In this way, it was possible to record in succession negativity from eight different points in less than 2 minutes.

After each experiment, the heart with strings attached was excised, preserved in formalin, and subsequently photographed (Fig. 2). From these photographs, outline sketches were made showing the exact location of the unipolar leads.

Owing to personal limitations of judgment and differences in hearts it was impossible to place ligatures absolutely in the same locations, consequently, certain areas were established for this entire series of experiments within which leads labled 1, 2, 3, etc. were placed (cf. Fig. 3). In the earlier experiments leads from eight such areas were taken, but in later experiments they were limited in number to six.

Interpretation of Direct Leads.—In order to interpret more readily the incidence of negativity at the individual points tested, the threads were connected to the galvanometer circuit so that the recorded curve rose when the points were negative.

Preliminary tests similar to those introduced by Lewis and his associates[12] indicated that, in this way, extrinsic deflections due to negativity elsewhere in the heart could be recognized as a downward de-

flection, and intrinsic effects by the sharp upward deflection. While there appears to be little question that the large, abrupt, positive deflections thus recorded indicate negativity at the points of lead, we may not necessarily assume that the very beginning of the rise represents the first moment of surface negativity; on the contrary, it is conceivable that the development of negativity in fibers lying at some depth directly below these points may induce negativity at the surface slightly in advance of the excitation wave.

This possibility had to be borne in mind in selecting the actual point in the intrinsic deflection record which could safely be regarded as a criterion of surface negativity, for when records are taken on rapidly moving paper it is frequently found that the ascending limb of what we interpret to be the intrinsic deflection is not a straight line but begins as a curve with slightly more gradual gradient. This is shown in many of the records reproduced but may be illustrated especially by reference to segments *C* and *D* of Figs. 5 and 6. Here the more gradual gradient *m*—*n* changes midway up the slope into a steeper gradient. This point *n* was used in all computations when the gradient was not absolutely smooth.*

ANALYSIS OF RESULTS

Analysis of Records.—The analysis of results may profitably be begun by the consideration of a number of specimen records showing the relation of initial negativity over various surface areas, and the rise of pressure within the ventricle.

Fig. 4 contains eight segments of records illustrating the relations of various direct leads to left (upper) and right (lower) intraventricular pressure changes, the eight points from which leads were derived corresponding to those indicated in Fig. 2.

As can clearly be seen in these records, the rise of the pressure in the left ventricle preceded that of the right (.0218 sec. by measurement). The beginning of the intrinsic negativity is clearly shown in all segments by the upstroke of the electrical variations from which lines are drawn. No parallax occurs between the two pressure records

*Since the foregoing was written an article by de Boer[21] has appeared, in which (p. 168) he brands the method employed by Lewis and his associates[12] for detecting surface negativity as "unreliable." Inasmuch as essentially the same procedure is used in this investigation, it becomes necessary to point out several errors of statement, which if left unchallenged might lead to misinterpretations:

1. A careful reading of the articles of Lewis and his associates[12] will reveal that they *did not* "assume that the biggest deflection was intrinsic"; on the contrary they established the probability by experimental data which it has been my privilege to corroborate.

2. The merest tyro in work of this sort should recognize that the unreliability of the method cannot be established by the mere fact that the distinctness of intrinsic deflection may be improved by changing the position of the indifferent electrode (!!). Yet this is the evidence (?) upon which de Boer bases his conclusion, "That this method is unreliable and that it cannot fix the instant of passage of an excitation wave over a given point on the ventricular wall."

3. The argument that conductivity is delayed over the thicker portions of the ventricle as found by Lewis and Rothschild [12] owing to a greater cooling of these surfaces is totally unsupported by any facts, and can be regarded only as an improbable hypothesis.

but the electrical records should be shifted to the right by .0024 sec. This was disregarded in drawing lines but taken into account in tabulated figures.

A comparison of the left intraventricular pressure curve (upper curve) with the surface negativity shows that the base of the left ventricle becomes negative slightly after the pressure rise (Record 1); the middle of the anterior surface of the left ventricle is negative simultaneously with this rise (Record 2); but the apex just above the vortex (Record 3) and the area to the left of the coronary sulcus (Record 4) are negative definitely before the pressure rises. All areas of the right ventricle are negative before left intraventricular pressure begins to be elevated (Records 5, 6, 7, 8). Inspection of these and succeeding segments of Fig. 4 shows at a glance that owing to the delay of right ventricular systole, all points of the cardiac surface are negative before the right ventricular pressure begins to rise. While this represents a case of extreme delay in the rise of right ventricular pressure, it is an experiment worthy of report as showing the possibility of the entire surface of the heart becoming negative before intraventricular pressure in the right ventricle even begins to rise.

The curves of Fig. 5 are introduced to cancel another possible criticism, namely, that the moment when intraventricular pressure rises cannot be accurately determined owing to the effect of auricular contraction, labeled *a* in Fig. 4. During the course of other observations in these experiments, we had occasion to test the effects of rebreathing air containing high percentages of CO_2. In one experiment this resulted in depression of A-V conductivity of such an order that it greatly prolonged the P-R and A_s-V_s intervals, thus causing auricular contraction far in advance of ventricular systole. In Fig. 5 this auricular contraction occurred during the wave labeled *a* and it is obvious that the pressure line before the rise of intraventricular pressure is absolutely even.

The four segments show electrical variations taken from areas 1, 3, 5, 7 (Fig. 3) together with aortic and intraventricular pressure curves. Owing to parallax, the electrical record should be shifted .0037 sec. to the right. Negativity at the left ventricular base occurs slightly after the rise of intraventricular pressure (Record A); but again the apex is negative earlier (Record B). Segments C and D show that negativity over the central and basal regions of the right ventricle (areas 5-7, Fig. 3) precedes the rise of the left ventricular pressure by considerable intervals.

A third series of illustrations taken on a very rapidly moving paper is shown in the segments of Fig. 6. A glance at these segments shows that negativity on the basal and middle surface of the ventricles (Records A and B) occurs a short interval after the pressure rise;

over the left apex and right central region, however, it definitely precedes this rise (Records C and D). Another point may also be developed in relation to these records. In a recent paper[18] I presented evidence that the initial rise of intraventricular tension (x-y) is probably due to the serial summation of fractionate contractions as the contraction process spreads over the ventricle, and that the abrupt rise of pressure after y does not occur until all ventricular fractions have begun to contract.

Since these experiments, as well as those of Lewis and Rothschild,[12] show that the left base develops negatively latest we should expect that the surface area "1" (Fig. 3) would not develop intrinsic negativity until the intraventricular pressure had developed to point y, provided electrical and mechanical processes are indeed due to the same causes. The relations, shown in segment A, indicate, however, that negativity precedes this point by .029 sec., indicating that contraction follows excitation by a later interval of approximately this duration.

Results of Different Experiments.—Calculations of data from records similar to those presented in detail were made on 44 different sets of records obtained from 21 different dogs. As the results are not exactly alike and as it is desirable to enter into the precise time relations, they are presented in Table I. A plus sign preceding a numeral indicates that negativity precedes, and a minus sign denotes that it follows the rise of left intraventricular pressure.

In the first column of figures is given the precedence of R_{II} already referred to earlier in the paper. We note that without exception it precedes the pressure rise in the left ventricle by .01 to .033 sec.

We may conveniently begin our analysis of negativity over various surface areas by a consideration of the relation which the pressure rise in the left ventricle has to negativity over "area 5" on the right ventricle. The significance of such comparisons may first be briefly stated, however. The experiments of Lewis and Rothschild[12] leave little question that the wave of negativity has spread over the entire ventricular septum, as well as over the papillary muscles of both ventricles, by the time that the earliest negativity appears over "the central area" of the right ventricle. Consequently, if these structures are contracting at the time this area is negative, we should expect that the left intraventricular pressure would certainly begin to rise by this time. The figures of Table I in the column labeled "area 5" show at a glance that this is not the case: on the contrary, this area is invariably negative before the pressure rises in the left ventricle. In the majority of experiments the interval of precedence is .013 to .031 sec.; in a small number it is consistently shorter (Exp. 352, 353, 366) probably because the leads were not placed at the points of earliest negativity (cf. also Fig. 2).

The relation of earliest surface negativity over the left ventricle to the rise of left intraventricular pressure is shown in the column labeled "area 3" in Table I. An analysis of 44 observations shows that in 19 cases, negativity of the left apex precedes the rise of pressure by

TABLE I

INTERVALS BETWEEN ELECTRICAL VARIATIONS AND LEFT INTRAVENTRICULAR PRESSURE RISE

EXPERIMENT		ECG	AREA 1	AREA 2	AREA 3	AREA 4	AREA 5
C 343	I		−.015		−.005	−.001	+.013
C 344	II	+.010	−.01	+.006	+.007		+.006
	III	+.011	−.009	+.006	+.011		+.013
C 345	I	+.024	+.002	+.002	+.003		+.020
C 346	I	+.025	−.006		+.001	+.006	+.019
C 347	II	+.023	−.010	−.005	−.002	+.005	+.020
C 348	I	+.020	0		−.003	+.016	+.026
	II	+.018	0		+.005	+.014	+.005
C 349	II	+.025			+.007		
C 350	I	+.025	−.007	0	+.016	+.002	+.026
	II	+.020	+.003		+.015	+.006	+.029
C 352	XII	+.015	−.008	−.002	+.006		+.009
C 353	II	+.011		−.006	−.001		
	XIII	+.015	−.01	0	−.005		+.007
C 354	II	+.028		+.015	0		+.021
	III	+.034		+.013	+.001		+.027
	VII	+.023		+.004	−.006		+.017
	VIII	+.021		0	−.003		+.017
	IX	+.025		0	−.002		+.019
C 356	I	+.026	−.009	−.004	+.003		+.009
	II	+.030	−.004	−.004	+.013		+.017
	III	+.033	−.004	+.003	+.011		+.021
	VII		−.002	+.001	+.011		+.021
C 357	II	+.010		−.005	−.005		+.016
C 358	I	+.027		−.008	0		
	II	+.031		−.008	−.004		
	III	+.029		−.011	0		+.019
	V			−.011	−.003		+.021
	IX	+.021		−.018	−.006		+.031
C 359	I	+.019			−.002		+.019
	II	+.017			−.004		+.016
C 361	IV	+.025		−.001	−.005		+.008
	VI	+.027		−.004	−.005		+.015
	IX				−.006		+.006
C 362	I	+.025		−.013	−.007		+.011
	II			−.004	−.007		+.015
C 363	I	+.019		−.002	+.002		+.014
C 364	I	+.021		−.005	−.004		+.017
	II	+.027		−.005			+.018
C 365	I	+.025		−.005	−.002		+.016
	II	+.025		−.005	0		+.016
C 366	II	+.023		+.002	+.007		+.007
	III	+.020		−.004	+.007		+.007
	IV	+.020		−.005	+.004		+.006
	V	+.025		−.005	+.007		+.008

.001 to .015 sec. and in 4 cases the two occur simultaneously. The evidence is clear that in none of these 23 cases is it possible to assume that mechanical and electrical responses are directly related. In 21 experiments, negativity over the apex surface followed the elevation of intraventricular pressure by .002 to .006 sec. It is my impression

that in these cases the ligatures from which leads were derived, were probably not placed so as to record the very earliest negativity at the apex, but we must accept the figures in an unqualified way. At first sight they are not so convincing as those of the other series, but a little consideration shows that they also corroborate the view that electrical and mechanical reactions cannot be identical. According to the data obtained by Lewis and Rothschild[12] it requires at least an interval of .01 sec. for the electrical wave to penetrate the muscle thickness at the apex, from endocardial to epicardial surfaces. Consequently, the internal layers also contract at least this much earlier than the external (cf. also Fig. 74, Lewis[10]). Inasmuch as the negative intervals never equal or exceed .01 sec., we must suppose that negativity in the internal lining under these points occurs definitely earlier than the rise of intraventricular pressure.

TABLE II

INTERVALS BETWEEN SURFACE NEGATIVITY OF THE RIGHT VENTRICLE, AND THE RIGHT INTRAVENTRICULAR PRESSURE RISE

EXPERIMENT		AREA 5	AREA 6	AREA 7	AREA 8
C 343	I	+.013	+.007	+.006	+.001
C 344	II	+.031		+.024	+.016
	III	+.030		+.020	+.008
C 345	I	+.020	0		+.004
C 346	I	+.019	+.003	+.017	
C 347	II	+.020	+.025	0	
C 348	I	+.026	+.026	+.016	+.003
	II	+.036	+.033	+.026	+.016
C 349	II	+.020			+.018
C 350	I	+.038	+.034	+.025	+.019
	II	+.041	+.035	+.027	+.025

An analysis of similar data of electrical negativity over "areas 2" and "1" toward the middle and basal portions of the left ventricle shows that a progressive increase of the negative intervals and a progressive decrease in the positive intervals occurs. In a total of 36 comparisons listed under "area 2" surface negativity still preceded the rise of left intraventricular pressure by .010 to .015 sec. in 9 cases; occurred simultaneously in 4 instances; and followed by .01 to .013 sec. in the remaining 23 cases.

In a total of 16 comparisons listed under "area 1," surface negativity still preceded in 2 cases; occurred simultaneously in 2 cases; and in the remainder followed by .001 to .015 sec.

There can be no question but that all of these values are definitely below the time required for the negativity waves to spread through the thicker ventricular walls of the more basal portions of the left ventricle. Such results are difficult to interpret if we assume that electrical and mechanical variations occur synchronously.

Evidence of a still more crucial character is obtained by comparisons of the surface negativity over the right ventricle with the rise of

right intraventricular pressure. This was done in 11 observations on 8 different animals where right and left intraventricular pressures were recorded simultaneously as in Fig. 4. The results of these experiments are given in Table II, the data in the column labeled areas 5, 6, 7, and 8 corresponding to those charted in Fig. 3. A perusal of these figures indicates that with only two exceptions—where surface negativity and mechanical events were synchronous—the electrical negativity had spread over the entire surface of the right ventricle, including the conus, before the right ventricular pressure had begun to rise. The intervals of precedence are longer in comparison made with the electrical changes in the central region (.02 to .041 sec.) and decrease progressively as the base of the right heart is approached.

SUMMARY

The interrelation or independence of electrical and contraction phenomena of the mammalian heart were studied in experiments in which the surface negativity on the ventricles and the rise of pressure within the ventricles were compared. Such comparisons were selected on the assumption that by the time intrinsic negativity appears on the surface of the ventricles, the whole interventricular septum and the entire thickness of ventricular wall at the point studied must have been excited; consequently, if electrical variations are an accompaniment of the contraction process, surface negativity should nowhere precede the rise of intraventricular tension and, in many places should follow at reasonable intervals.

Anatomical and experimental facts are reviewed which indicate (a) that the manometers record intraventricular pressure without lag, (b) that the rise of intraventricular pressure is a certain index of the initial contraction, and (c) that surface negativity can be determined with reasonable accuracy by unipolar leads.

The observation of Lewis and Rothschild[12] that surface negativity develops earliest over the central region of the right ventricle is confirmed. By this time we have ample reasons to suppose that the wave of negativity has spread over the entire interventricular septum which, according to anatomical considerations, should be capable of elevating intraventricular pressure by the contraction of its circular fibers. Actual results show, however, that negativity over this region precedes the elevation of right ventricular pressure by .02 to .041 sec. and the rise of the left intraventricular pressure by .013 to .031 sec.

The earliest negativity over the left ventricle was found to occur over the apex, again confirming the results of Lewis and Rothschild.[12] By this time the wave of negativity has spread not only over the interventricular septum and left papillary muscles, but has penetrated the entire thickness of the left ventricular apex. Comparisons of surface negativity with the elevation of left intraventricular pressure showed

that in half of the experiments the former preceded by .001 to 0.15 sec., and in the other half followed by .002 to .006 sec. As these intervals are shorter than the probable time required for the wave of negativity to pentrate the wall of the apex, these results also indicate that electrical and contraction processes cannot be simultaneous in the dog's heart.

In a general way, the wave of negativity appears later on the surface of the ventricles as the bases are approached. Consequently, negativity appears relatively later as regards the elevation of intraventricular tension on the two sides. In the case of the right ventricle this merely has the effect of reducing the interval of electrical precedence, negativity still preceding the elevation of intraventricular tension by .006 to .027 sec. In the case of the left ventricle, the relatively earlier beginning of the pressure rise and the longer time of conduction combine so that the negativity of the left basal surface as a rule follows the elevation of intraventricular tension by .002 to .015 sec.; in a few instances, however, negativity still precedes by .002 to .003 sec.

Such results taken separately or conjointly cannot be explained by assuming a synchronicity of electrical and mechanical processes in the dog's ventricle; on the contrary, they distinctly favor the view that electrical variations are an accompaniment of impulse conduction which precedes the actual contraction process by a definite interval.

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GONOCOCCIC BACTEREMIA WITH GONOCOCCIC ENDOCARDITIS AND AORTITIS*

A Case Report

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THE relation of the rheumatic virus to the etiology of heart disease has been appreciated for a long time but it has been only during the past twenty-five years that the attention of clinicians has been drawn to the gonococcus as an agent occasionally injurious to the heart. There are now in the literature about eighty instances of gonococcic infection of the endocardium.

There are many questions about the disease which await solution and these are concerned with both its pathological and its clinical recognition. The following case is reported because of several unusual features which it presents and because it illustrates the difficulties which are encountered in attempting to establish the clinical diagnosis of gonococcic endocarditis in a suspected case.

SUMMARY OF THE CASE

A Swedish boy, twenty-two years of age, was admitted to the hospital complaining of shortness of breath, cough, and swelling of the limbs. A history of rheumatism or chorea could not be obtained. He had had scarlet fever and diphtheria before the age of ten. He had been refused admission to the Navy at the age of twenty because of alleged heart disease. He went to sea in 1921, and in December, 1924, contracted gonorrhea. Treatment was started at once for this condition and no evidence of it could be found when he entered the hospital. Early in February, 1925, seven weeks after the onset of gonorrhea, he "caught cold in his chest." At this time he had some discomfort in his chest, became very thirsty and had chills, but had no pain in his joints. He remained at work for a few days but soon noticed that his feet, ankles, and finally his face, were becoming swollen. He was constantly fatigued, and was short of breath on exertion. He went to a hospital (February 25) where he remained twenty-four days. At this institution he was treated for acute nephritis. However, his condition did not improve and he was admitted to the New York Hospital on March 21.

The physical examination on admission showed a well-developed young man lying propped up in bed, in acute respiratory distress. There was general anasarca. The skin had a yellowish appearance, there was a slight protrusion of the eyes and a marked pallor of the mucous membranes—all of which presented a striking picture. A petechia could be seen on the left conjunctiva. The ophthalmoscopic examination showed only retinal edema. The voice was extremely hoarse and the patient talked in a whisper. There was a slight inspiratory stridor; the neck pulsations were accentuated; the respiratory rate rapid. There was impairment of resonance at the left base posteriorly, with a small area of tubular breathing. The

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precordial dullness was greatly increased to the left and downward and moderately to the right. There was a diffuse wavy impulse over the precordium. The maximum impulse could be seen 10 cm. from the midsternal line in the 5th interspace, and the left border of cardiac dullness in the 5th interspace appeared to be about 14 cm. from the midsternal line, near the anterior axillary line, a distance of 4 cm. from the point of maximum impulse. The aortic arch dullness measured 8 cm. The first sound at the apex was loud and rough, accompanied by a systolic murmur which could be heard over the entire precordium. Over the sternal area there was

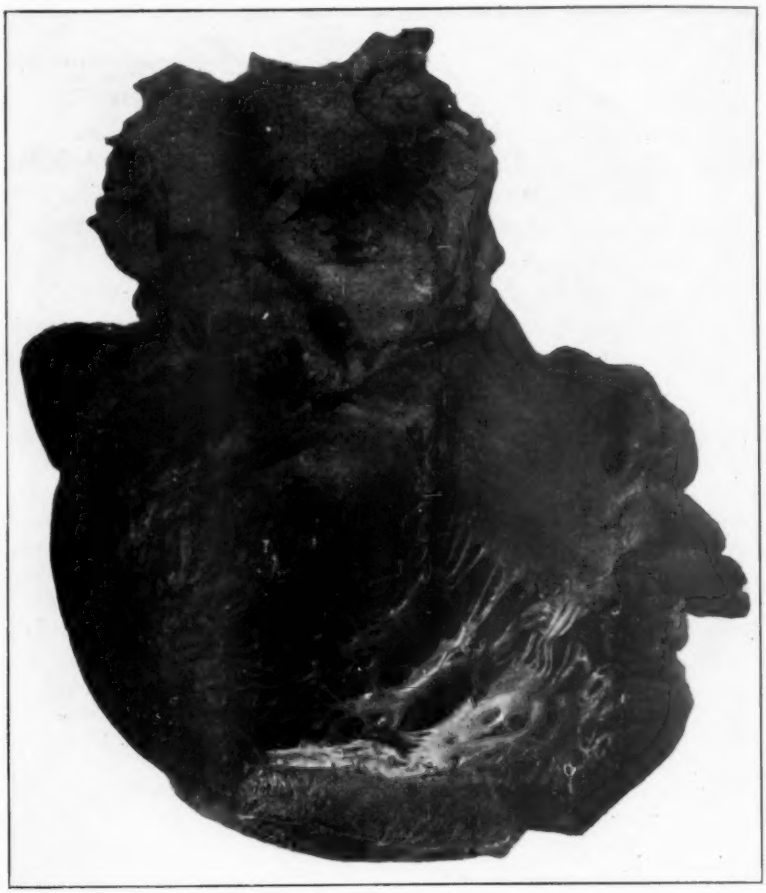

Fig. 1.

a fairly loud to and fro friction murmur. The second pulmonic sound was loud and snapping. There was a distinct diastolic murmur over the aortic area. The outline of percussion dullness and the friction sound indicated a pericardial effusion. There were definite signs of aortic insufficiency. The liver was moderately enlarged, and the spleen palpable. The pulses were moderately collapsing in type.

Laboratory examinations were as follows: Urine turbid, highest specific gravity 1.018. There were present a cloud of albumin, considerable pus, and occasional red blood cells. Blood—red cells were 3.7 millions, with hemoglobin 48 per cent; white cells 33,500, 94 per cent polynuclears. The Wassermann reaction was negative. The icterus index was normal (5.1), the blood urea nitrogen varied from 78 to 94

mg. per 100 c.c.; the creatinine was 3 mg. per 100 c.c. Smears from the pus in the urine revealed no organisms, and the three-glass test showed the same amount of pus in each specimen.

The blood culture, taken on admission, showed gonococci in the liquid cultures. The agar plate cultures yielded negative results. This is a common experience with this type of organism. The cultural media employed in this instance were two plain agar plates and 100 c.c. each of plain broth and glucose calcium carbonate broth; adding to each 5 c.c. of blood. The organisms were recovered in both broth cultures. Had we relied upon agar plates alone in culturing the blood the diagnosis would have remained obscure. The organisms isolated from the broth bottles were identified as gonococci by staining cultural, and fermentation methods.

The electrocardiogram showed a normal sinus rhythm, with right ventricular predominance. The blood pressure remained uniformly low, 110/70. The temperature was of the intermittent and remittent type, varying from 100 to 103½, the terminal temperature being 105. The pulse rate was constantly above 110 and at times as high as 158 per minute.

The heart was digitalized immediately but fluids were not limited. There was a loss in weight of 10 pounds during the course of five days, which was probably due to the marked diuresis which occurred during digitalis therapy. The patient did not improve however. He complained of pain over the precordium, headache, and increasing weakness. Five days after admission he died.

Necropsy was performed twelve hours after death. The lungs showed bronchopneumonia at the lower left base, cultures of which yielded a hemolytic streptococcus. There was a small amount of fluid in each pleural cavity. The pericardium contained about 300 c.c. of purulent brownish fluid and the pericardial surfaces were covered with fibrinous exudate. Smears from the fluid showed numerous pus cells but no organisms, and cultures of the fluid gave no growth. The heart itself was markedly hypertrophied, weighing with the pericardium 1075 grams. The pulmonary, mitral, and tricuspid valves were normal. The aortic valve had the appearance of old disease, as evidenced by a considerable thickening and retraction of the cusps. At the edge of the left posterior cusp there was a small friable grayish-white vegetation. This was clipped off and cultured; the culture yielding only a hemolytic streptococcus. About 4 cm. above the base of the aorta there was a more or less circular opening in the aortic wall measuring about 2 cm. in diameter. This led into an irregular cavity about the size of a lemon. The cavity closely simulated a sacculated aneurysm. Upon closer inspection it was found that the lining of this sac consisted of pericardium. The condition found was due to an ulceration of the aorta, with perforation into a walled-off portion of the pericardial sac. The process was then mycotic aortitis with perforation. About the opening of the aneurysmal sac there were several small friable vegetations similar to the one on the aortic cusp. Gonococci could not be cultivated from these vegetations and microscopic sections through them failed to show organisms. The kidneys were the large white type, with evidence of chronic and acute nephritis, and there were several old and recent infarcts. The spleen was fairly large, weighing 426 grams. It contained several old white infarcts. The liver was somewhat enlarged by chronic passive congestion. The prostate was normal microscopically; no cultures were made from it. Cultures of the kidney tissue gave staphylococci and hemolytic streptococci as the only organisms. There was no abscess formation in the infarctions. The postmortem blood cultures showed hemolytic streptococci; no gonococci.

In summary, the case was one of gonococcic endocarditis, gonococcic bacteremia with terminal hemolytic streptococcic bacteremia and septicemia, superimposed upon chronic endocarditis. The time of onset

of symptoms was about two months after the appearance of acute urethritis. The clinical diagnosis was confirmed by positive broth blood cultures for gonococci taken five days before death, and by necrospy findings, all of which were characteristic of the disease.

DISCUSSION

The principal interest in the case was the presence of mycotic aortitis, with rupture of the aorta into the pericardium, the etiological factor being the gonococcus. It is also noteworthy that the diagnosis rests upon a single antemortem blood culture, although the pathologist was able to anticipate the diagnosis at necropsy without this information.

The finding of the Streptococcus hemolyticus in the postmortem cultures might appear to cast doubt upon the diagnosis. As far as can be determined, no cases of mycotic aortitis caused by the hemolytic streptococcus have been reported in the literature. The organism is frequently present in the blood stream, and any pronounced tendency to cause lesions similar to those present in this case would certainly have been noted. Had the gonococcus not been recovered by the blood culture during life it would have been necessary to disregard the presence of the hemolytic streptococcus in the postmortem cultures and look elsewhere for the cause of death. The pathological findings would strongly have suggested the gonococcus or meningococcus as the probable invading organism. The cultivation of an hemolytic streptococcus from the vegetations was merely an expression of their presence in the blood stream.

The presence of a purulent pericarditis with sterile cultures does not detract from the fact that this condition was due to gonococcus infection. In this respect it is interesting to note that in cases of meningococcic pericarditis the cultures are often sterile. Elser[1] was unable to recover the meningococcus from the pericardial fluid in three cases of general meningococcic infection with complicating purulent pericarditis, although in one case the organisms were demonstrated bacterioscopically. It is also true that the pneumococcus may die out in old pericardial exudate. Meakin[2] states that pericarditis is always present in gonorrheal endocarditis, but in Thayer's[3] series its presence was noted in only 20 per cent of the cases.

The question of the occurrence of *acute* bacterial endocarditis on heart valves not previously diseased has never been satisfactorily settled. In this case there was evidence, both historical and anatomical, of preexisting aortic valvular disease. The aortic valves were thickened and the heart itself showed more hypertrophy than could have been caused by an endocarditis of recent onset.

Aortitis and mycotic arteritis have been described in endocarditis caused by the Streptococcus viridans, the gonococcus, and the Micro-

coccus zymogenes. The relative frequency is about in the order named. The hemolytic streptococcus has never been shown to be an etiological factor in the production of these lesions. In the case here reported the appearance of the aneurysm was somewhat deceptive because of its location and contour, but microscopic sections showed that the lining of the sac consisted of pericardium rather than sacculated wall of the aorta.

The severe nephritis, which was a prominent feature in this case, is common in gonococcic endocarditis although not sufficiently so to make it of diagnostic importance. According to Libman[4] severe forms of nephritis are common in other forms of bacterial endocarditis. Embolic phenomena were present in this case but they are in no way diagnostic of the type of endocarditis.

The high leucocyte count which was constantly present, is also characteristic of the disease in general but it is of little diagnostic importance. In cases of subacute bacterial endocarditis, a leucocytosis is frequently present during complications, such as infarcts, and in gonococcic endocarditis severe complications are common and may be accountable for the high leucocytosis.

From a clinical standpoint the differential diagnosis between the various forms of endocarditis is difficult. The positive diagnosis of gonococcic endocarditis can be made only by the recovery of the organism from the blood stream. The high leucocyte count, not infrequent pericarditis, and usually severe nephritis, as well as the generally severe and rapidly fatal course of the disease are all characteristic features, but they may occur in other types of endocarditis, particularly among those of the staphylococcus and pneumococcus groups. The presence, or recent history, of gonorrheal urethritis is only presumptive evidence and cannot be said to exclude other organisms as etiological factors. Acute urethritis is extremely common and its presence in cases of meningitis or bacterial endocarditis is not alone proof that the gonococcus is the cause of the disease in each case.

I am indebted to Dr. Lewis A. Conner for permission to report this case and to Dr. Nellis B. Foster and Dr. Wm. J. Elser for helpful criticism.

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THE VALUE OF THE X-RAY IN DETERMINING THE CAUSE OF AORTIC REGURGITATION*

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INTRODUCTION

AORTIC regurgitation may result from the following conditions: first, "rheumatic" endocarditis with ulceration, fibrosis and contracture of the valve leaflets; second, syphilitic ulceration and erosion of the valves or dilatation of the aortic ring in aneurysm of the ascending aorta; third, arteriosclerosis of the aorta when there is imperfect closure of the leaflets; fourth, rarely hypertensive heart disease with functional dilatation of the aorta and aortic ring; fifth, occasionally severe anemia; and sixth, but rarely, trauma. Ordinarily the cause is evident and we are able to place it under one of these headings and sometimes under more than one.

There are cases of aortic regurgitation, however, which are puzzling etiologically and in which one seeks the aid of all methods in differentiating them, because the prognosis to a considerable extent depends upon the etiology. For example, syphilitic aortic regurgitation is a very serious condition and generally means death in a few months or a few years at the best, even if diagnosed early, while rheumatic aortic regurgitation in the absence of heart failure may be borne for twenty or thirty years. Now and then in routine examination (as for insurance) an aortic diastolic murmur is discovered in a middle-aged person otherwise apparently healthy. It is of great importance to determine the etiology of this aortic regurgitation. The value of the x-ray in such a case aroused our interest in the subject and occasioned the present investigation.

An editorial in the *American Journal of Roentgenology* in 1922[1] called attention to the fact that the x-ray is accepted for the detection of aneurysm, but is used to a less extent for the estimation of the size of the heart and study of the great vessels. The writer of the editorial felt that it was undue conservatism that impeded the use of the x-ray in the study of the heart. Our investigation of the literature since that time has shown us that this is still more or less true. This fact enhances the value of the report of our findings.

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LITERATURE

In a survey of the literature it becomes evident that the chief study of the heart and aorta by the x-ray is of foreign origin. Groedel[2] and Vaquez and Bordet[3] have written excellent textbooks concerning the use of the x-ray in the study of the normal and pathological heart and aorta. Both books stress the value of studying the aorta in all views. Neither one, however, has discussed satisfactorily the differential diagnosis of aortic regurgitation. Wessler and Jaches[4] pointed out the value of early roentgen diagnosis of syphilitic processes in the aorta before aneurysms form or the aortic valves become involved. Brown[5] and Elliott[6] emphasized the value of the x-ray in early diagnosis, and the latter went so far as to say that, with modern methods, we are guilty of neglect if we do not routinely examine the aorta in syphilitic patients. The Beretervides[7] have studied 77 orthodiagrams taken in 52 children with inherited syphilis and compared them with those of healthy children, and have found an abnormally large diameter of the ascending aorta in syphilitic children, which they believed is marked enough to be termed a new finding in congenital syphilis. Gluck[8] reported the death of an infant aged twenty months from intrapericardial rupture of an aortic aneurysm. However, neither the Beretervides nor Gluck mentioned aortic regurgitation of syphilitic origin in children, and in going over the records at the Massachusetts General Hospital, we have not found such a case. Symmers and Wallace,[9] and Symmers,[10] and many others have pointed out the frequency with which the aorta is attacked in syphilis. Pappenheimer and Von Glahn,[11] who gave Klotz credit for being the first to give serious study to the histological lesions in the aorta resulting from rheumatic fever, have also made careful observations and have found considerable pathological change in the walls of the aorta, undoubtedly due to acute rheumatic fever. Clinical study of the aorta by x-ray would have been of interest in their series, since Deusch[12] wrote that in very rare cases tuberculosis and articular rheumatism may produce such changes in the arterial wall that there results dilatation which may be shown by x-ray. Deusch (agreeing with Romberg) felt that striking enlargement of the ascending aorta is not unusual in any marked aortic regurgitation, and that it is the result of the continued expansion of the vessel wall from the rise in blood pressure, as a result of which there occur early sclerotic changes in the vessel wall and loss of elasticity. He felt also that there is the possibility of a functional dilatation of the aorta during life which is not found postmortem. Allbutt[13] writing in 1915 expressed hope that the x-ray would be a means of successfully determining diseases of the aorta. MacIlwaine[14] stated that x-ray examination in most cases of aortic endocarditis of a syphilitic nature showed enlargement

of the aorta. Deneke[15] insisted that the differentiation of arteriosclerotic and syphilitic aortic disease is readily determined by studying the aorta in all diameters. He warned that they may coexist but should be differentiated. Boden[16] thought it easy to find calcareous plaques in the aorta with arteriosclerosis. He demonstrated them in 9 out of 36 patients between the ages of fifty and seventy years. Karshner and Kennicott[17] mentioned the value of the x-ray in the differential diagnosis of aortic involvement in hypertension, arteriosclerosis, senility, syphilis and rheumatic aortic regurgitation. They preferred fluoroscopic examination to the teleoroentgenogram in the study of the aorta.

PRESENT INVESTIGATION

In the present series a total of 34 cases of aortic regurgitation taken from the records of the Massachusetts General Hospital were studied. Of these 34 cases, 13 were syphilitic (Table I), 6 arteriosclerotic and hypertensive (Table II), and 5 rheumatic aortic regurgitation without other valvular disease (Table III). The remaining 10 cases were rheumatic aortic regurgitation plus mitral valve involvement in the form of stenosis or regurgitation or both (Table IV). All the cases with the exception of the last 10 were selected because there was some question of etiology. In the accompanying tables the age, sex, past history (briefly), blood pressure, Wassermann reaction and electrocardiogram (where taken) are correlated with the clinical and x-ray conclusions. Each type will be taken up and discussed independently. Aortic regurgitation due to anemia or trauma is not included in this series, since it is very rare.

We shall discuss the technic of our mode of examining the heart and great vessels by the x-ray, and what we consider the salient differential points in a given case of aortic regurgitation.

Technic.—The x-ray examination of the heart and great vessels as carried out at the Massachusetts General Hospital consists of a fluoroscopic study, preferably with the patient in the upright position, and one or more plates taken at a 7-foot target skin distance. In the fluoroscopic examination observations include anteroposterior, posteroanterior, right lateral oblique, and left lateral oblique views. The movements of the heart and diaphragm during respiration are noted, and a tracing of the heart and great vessels made both in the anteroposterior and in the lateral views. In taking the plates especial care is observed in placing the patient, and in focusing the tube. The tube is focused over the base of the heart shadow, with its central ray at right angles to the transverse diameter of the chest. The patient sits erect, and the cassette containing the film is placed against the anterior chest wall. If the patient leans forward, as is customary in the taking of chest plates, there is some slumping of the heart, and con-

sequent distortion of the shadow. The exposure is made during quiet breathing. Plates taken during full inspiration show an abnormally small heart shadow and a straightened-out aorta, due to the downward excursion and rotation of the heart. The exposure time should occupy at least one second, so that the picture obtained will be of the heart in diastole. It is best to use a film with double screens and a higher voltage and slightly longer exposure time than that used in the taking of ordinary chest plates.

From the x-ray examination, it should be possible to state (1) the size and shape of the shadow of the heart and great vessels both in the anteroposterior and in the lateral views, (2) the presence or absence of abnormal pulsations or masses, (3) the character of the pulsations of the various chambers of the heart and (4) the respiratory excursion of the heart.

The differentiation of the various types of aortic regurgitation by x-ray is based largely upon the shape of the heart shadow and upon the presence or absence of dilatation of the aorta.

In *rheumatic aortic regurgitation* without other valvular disease the shape of the heart shadow is fairly characteristic. The curve of the left ventricle is distinct. The increase in size varies somewhat in degree, but is always entirely to the left. The aortic shadow is normal in all views. When other valves than the aortic are involved or when dilatation of the auricles takes place, the increase in size becomes general and the interpretation must be based largely upon the appearance of the aorta. In these late or complicated cases the value of the x-ray finding is much diminished.

In *aortic regurgitation of syphilitic origin* the x-ray findings to be looked for are (1) an increase in the supracardiac shadow, which is usually found just above the heart shadow, to the right of the sternum in the region of the aortic valve, (2) abnormal pulsations in the region of the ascending aorta, (3) a cone-shaped supracardiac shadow, (4) a flattened aortic knob, (5) pyramid-like shadows extending upward from the aorta in the region of the innominate and subclavian arteries, and (6) changes in the appearance of the heart shadow,—either a moderate general enlargement accompanied by a poorly defined left ventricle and flabby beat, or a marked enlargement of the left side of the heart, with a blunt apex and horizontal position.

In *arteriosclerosis with aortic regurgitation* the enlargement of the heart may not differ from that of the syphilitic type, but the aorta is tortuous rather than dilated, so that in the oblique view the actual diameter of the ascending aorta is not increased, although there may be marked increase in the supracardiac dulness in the anteroposterior view. The aortic knob is prominent, not flattened as in syphilitic aortitis, and calcified plaques may be visible.

With the rare functional *aortic regurgitation in hypertensive heart disease* there is always some enlargement of the heart. In comparison with the syphilitic heart, the hypertensive heart is the more sharply defined, and the outlines of the various chambers are more distinct. The enlargement of the aortic shadow is usually manifest as a diffuse dilatation of the entire aorta. It may or may not show evidence of arteriosclerosis.

An unusually high diaphragm may also produce an increase in supracardiac dulness. This condition, however, is not accompanied

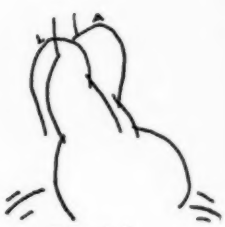

Fig. 1-*A*.

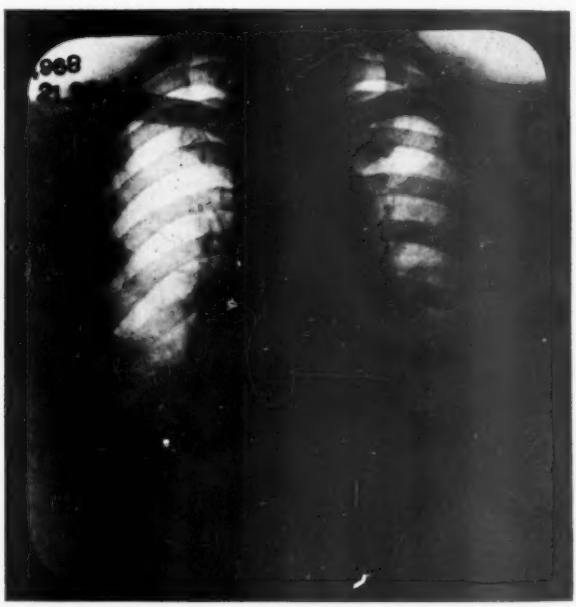

Fig. 1-*B*.

Fig. 1-*A*.—Case P. P. (*see* Table I). Syphilitic heart disease, with involvement of the aorta and aortic valve. The enlargement of the heart is downward and to the left, and is confined to the region of the left ventricle. The supracardiac shadow is increased both in the anteroposterior and in the lateral views. The aorta is also prominent in its ascending portion, and there is a shadow extending upward from the arch, which suggests dilatation at the junction of the innominate artery.

NOTE. *A*, anteroposterior view. *L*, lateral view of aorta (and great vessels). These signs refer to the following figures also.

Fig. 1-*B*.—Teleoroentgenogram. Case P. P. from Table I.

by any change in the heart itself, or by actual increase in the diameter of the aorta.

CASES

Syphilitic aortic regurgitation (see Table I). Of these 13 cases, 11, or 84.6 per cent, had positive Wassermann reactions, 2, or 15.4 per cent, negative. From the standpoint of the Wassermann reactions alone the x-ray was of great value in those two cases with negative reactions, aged forty and forty-five years, at a time when it is most

TABLE I

THIRTEEN CASES OF SYPHILITIC HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTROCARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS* BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
E. Med. 248587	M 40	Hard chancre 23 years ago, logically treated. Pharyngeal syphilis 14 years ago; nasal syphilis 12 years ago; mercurial treatment.	140/60	Negative repeatedly.	No axis deviation; sinoauricular tachycardia. Rate 120; inverted T2.	Mar., 1922.	R= 5.4; B=11.4; L=10.4; V= 7.8; T=15.8; l=17.0; Chest=28.0.	Heart generally enlarged; prominent left ventricle; increased supracardiac dulness, greatest prominence to the right. Impression: **syphilitic aortitis.**	**Syphilitic heart disease** with aortic regurgitation.
E. Med. 248495	M 38	Scarlet fever and tonsillitis as a child.	140/20	Strongly positive.		Mar., 1922.	R= 5.8; B=13.0; L=11.5; V= 7.8; T=17.3; l=18.0; Chest=25.3.	All chambers enlarged; greatest increase downward and to the left; supracardiac dulness increased. Aorta dilated in both anteroposterior and lateral positions.	**Syphilitic heart disease** with marked aortic regurgitation.
E. Med. 249401	M 53	Peritonsillar abscess and tonsillectomy 15 years ago; denies syphilis.	154/20	Strongly positive.		April, 1922.	R= 5.0; B=11.0; L= 8.5; V= 7.5; T=13.5; l=14.5.	Enlarged left ventricle. Dilated arch. **Syphilitic aortitis (?)** and aortic regurgitation?	Aortic regurgitation, **syphilitic.** Acute infectious jaundice.
E. Med. 249652	F 58	No rheumatic history; deafness and blurred vision for 2 years.	146/40	Strongly positive.		May, 1922.	R= 4.7; L= 8.1; V= 6.2; T=12.8; Chest=22.8.	Heart appears enlarged. Supracardiac shadow increased. Aorta tortuous with prominent knob, probably **arteriosclerotic.**	**Syphilitic heart disease** with slight aortic regurgitation; heart not very much enlarged.
E. Med. 249082	F 45	No infectious diseases. Previous good health.	130/40	Strongly positive.		April, 1922.	R= 4.1; B=12.3; L=11.0; V= 7.5; T=15.1; l=16.0; Chest=24.1.	Heart shadow appears enlarged to the left in the region of left ventricle. Supracardiac dulness increased in both views: **syphilitic aortitis.**	**Cardiac syphilis** with aortic regurgitation.

*Under heart measurements.
"R" is the right median diameter.
"L" is the left median diameter.
"T" is the total transverse diameter.
"B" is the total diameter at the base.
"V" is the diameter of the great vessels.
"T" is the length of the heart.
"Chest" is the internal diameter of the chest.

TABLE I—CONT'D

THIRTEEN CASES OF SYPHILITIC HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTRO-CARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
E. Med. 250195	M 45	Small penile sore 20 years ago. Scarlet fever at age of 4 years.	103/50	Negative repeatedly.		June, 1923.	R= 4.6; B= 9.5; L= 9.7; V= 7.1; T=14.3; I=15.2; Chest=25.6	Heart generally enlarged, particularly in region of left ventricle. Supracardiac dulness increased, aorta prominent to the right and left—also in the oblique view. Probably **syphilitic aortitis.**	**Syphilitic heart disease** with aortitis and aortic regurgitation.
III S. 259608	M 53	Diphtheria at age of 14. Gonorrhea in youth. Denies chancre. Influenza in 1918.	146/44	Strongly positive.	Nov. 1923: Normal rhythm; Rate 84; left axis deviation; index=+35.	1922.	R= 5.3; B=12; L= 8.7; V= 6.1; T=14.0; I=15.7; Chest=27.7.	Slight enlargement of the heart and dilatation of the aorta.	**Syphilitic heart disease;** aortic insufficiency; aortitis; angina pectoris. (Left cervical sympathectomy Nov. 21, 1923 without relief of pain: died July 6, 1924.)
						Oct., 1923.	R= 4.5; B=12; L= 9.5; V= 6.9; T=14.0; I=15.7; Chest=26.7.	Increase in the aortic shadow with prominence of the ascending aorta. Heart enlarged particularly in region of left ventricle. **Syphilitic aortitis.**	
O. P. D. 542172	M 35	No rheumatic infections. Denies venereal disease.	135/25	Strongly positive.		Aug., 1924.	R= 6.5; B=13.0; L=10.0; V= 9.0; T=16.5; I=18.0; Chest=28.0.	Heart increased in size, particularly in region of left ventricle. Supracardiac dulness increased to the right at ascending portion of aorta—also definite increase in oblique view. **Syphilitic aortitis.**	**Syphilitic heart disease;** aortic regurgitation; aortic pain.
O. P. D. 533605	F 34	Two attacks of peritonsilar abscess five years ago. No other infections.	180/0?	Strongly positive.		May, 1924.	R= 4.5; B=10.0; L= 8.5; V= 6.5; T=13.0; I=14.0; Chest=24.5.	Heart shadow enlarged down and to the left. Slight prominent supracardiac dulness which is also prominent in the oblique view. **Syphilitic aortitis.**	**Syphilitic heart disease** with aortic regurgitation.
O. P. D. 557169	M 58	Primary lesion twenty years ago followed by "secondaries." No treatment.	164/64	Strongly positive.		Jan., 1925.	R= 4.0; B= 8.3; L=11.5; V= 7.2; T=15.5; I=16.4; Chest=25.0.	Heart shadow enlarged. Increase is down and to the left. Marked increase in supracardiac shadow in both ant.-post. and lateral views. Aortic knob prominent. Imp: Arteriosclerosis with dilatation due to **syphilis or hypertension.**	**Syphilitic and arteriosclerotic heart disease** with aortic regurgitation, aortitis and angina pectoris.

TABLE I—CONT'D

THIRTEEN CASES OF SYPHILITIC HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTROCARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS* BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
O. P. D. 514417	M 64	Rheumatism 6 years ago of 5 months' duration. Denies venereal disease.	150/58	Strongly positive.		Oct., 1923.	R= 5.0; B=11.0; L=10.0; V= 6.5; T=15.0; I=16.0; Chest=24.7.	Heart shadow increased in size. Enlargement in region of left ventricle. Also some increase in supracardiac dulness. Rather prominent aortic knob. Imp: **Enlarged heart and dilated arch.**	**Syphilitic heart disease; syphilitic aortitis;** aortic regurgitation.
O. P. D. 523470	M 51	"Never sick before."	164/50	Moderately positive.		Jan., 1924.	R= 6.2; B=11.5; L=10.2; V= 7.0; T=16.4; I=17.1; Chest=26.5.	Heart shadow increased both to the right and to the left. Supracardiac shadow increased in the anteroposterior view particularly to the right. Probably **syphilitic heart.**	**Syphilitic heart disease** with aortic regurgitation.
P. P.	M 52	Malaria at 18; nervous prostration 12-14 years ago.	170/65	Strongly positive.	Normal rhythm; rate 90.	April, 1925.	R= 3.5; B= 8.0; L=11.0; V= 8.0; T=14.5; I=15.0; Chest=27.0.	Heart somewhat enlarged to the left; no unusual pulsations. Supracardiac dulness increased—aorta prominent in both anteroposterior and lateral views. Ascending portion of knob slightly prominent, and there is a shadow suggesting dilatation of the innominate. Imp: hyp. left ventricle, **dilatation and tortuosity of aorta probably due to syphilis.**	**Syphilitic heart disease;** aortic regurgitation and aortitis. (See Figs. 1-*A* and 1-*B*.)

important to make a diagnosis. It is well to mention here that conversely a positive Wassermann reaction with aortic regurgitation does not mean necessarily that the aortic process is syphilitic. Rheumatic endocarditis with incidental lues may be present.

The average systolic blood pressure in these 13 cases was 147 mm. and the average diastolic presure 41 mm. Thus it seems that here, instead of a high systolic, it is a high pulse pressure that further dilates a diseased and weakened aortic wall. In case O.P.D. 523470 there was an undoubted Austin Flint murmur which in all respects is identical with the murmur of mitral stenosis. Had this been interpreted as a murmur of true mitral stenosis, according to some ob-

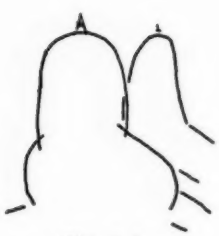

Fig. 2-A.

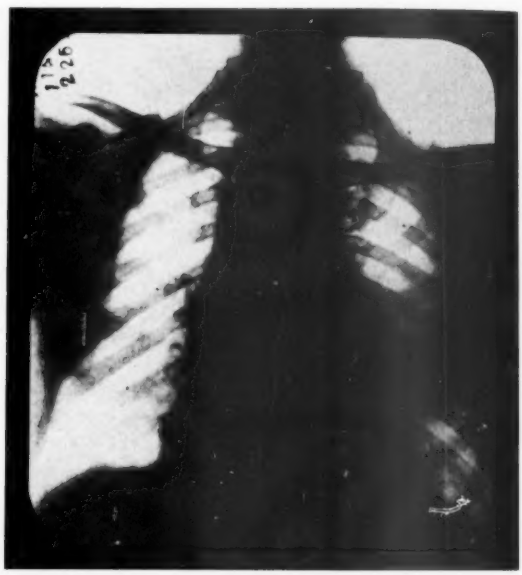

Fig. 2-B.

Fig. 2-*A*.—Case O. P. D., 528637 (*see* Table II). Advanced arteriosclerosis with hypertension and aortic regurgitation. The heart shadow is enlarged to the left in the region of the left ventricle. There is also a marked increase in the supracardiac shadow, but in the oblique view there is no definite increase in the size of the aortic shadow. The increase in the supracardiac shadow is due largely to the tortuosity of the aorta.

Fig. 2-*B*.—Teleoroentgenogram. Case O. P. D. 528637 from Table II.

servers, this would have meant rheumatic heart disease; here the x-ray clearly demonstrated syphilitic aortitis. The x-ray and clinical interpretations differ in O.P.D. 557169; this illustrates the difficulty that one may meet when arteriosclerosis and syphilis are combined. Ordinarily syphilitic heart disease manifests itself before the arteriosclerotic age, yet it is well to remember that it may be seen earlier or later in life, depending on when the infection was acquired. The last case in this series P.P. (see Fig. 1 and Fig. 1-*A*) had been under the care of two excellent internists for several years, and a few

TABLE II

SIX CASES OF ARTERIOSCLEROTIC AND HYPERTENSIVE HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTROCARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
W. Med. 254044	M 70	Ordinary diseases of childhood.	200/60	Negative.	Marked left axis deviation +40 by index, - 55° by angle; V.P.B.	Jan., 1923.	R= 5.9; B=12.7; L=11.0; V=10.2; T=16.9; l=16.1; Chest=24.5.	Large left ventricle. Tortuous aorta, very wide anteroposteriorly, but normal laterally. Imp: **"arteriosclerotic."**	**Arteriosclerotic and hypertensive heart disease** with aortic regurgitation.
W. Med. 254248	F 69	Rheumatic fever five years ago; pneumonia 3 years ago.	210/80	Negative.	Sinoauricular tachycardia; rate 110; diphasic T2.	Feb., 1923.	R= 3.2; B=11.1; L= 8.5; V= 6.0; T=11.7; l=13.4; Chest=20.5.	Heart shadow enlarged, almost entirely to the left. Supracardiac dulness increased anteroposteriorly, but normal in oblique plane. Appearance that of **Arteriosclerosis.**	**Arteriosclerotic and hypertensive heart disease** with aortic regurgitation, angina pectoris and coronary sclerosis.
W. Med. 254233	F 40	Negative.	240/142	Negative.	Normal rhythm; rate 80; inv. T2; marked left axis deviation.	Feb., 1923.	R= 8.7; B=11.7; L=12.2; V= 6.8; T=20.9; l=19.1; Chest=29.7.	Heart shadow much enlarged; pulsations not diminished. Aortic knob prominent. Aorta seems large in both views. All chambers dilated.	**Hypertensive and arteriosclerotic heart disease** with aortic regurgitation; chronic nephritis and hypertension.
E. Med. 255245	M 52	Gonorrhea as a boy; syphilis denied; no rheumatic fever; occasional tonsillitis. Erysipelas 20 years ago.	146/110	Negative.		Mar., 1923.	R= 8.5; B=12.5; L=12.7; V= 8.2; T=21.2; l=20.2; Chest=31.1.	Cardiac shadow definitely enlarged to the right and left. Supracardiac dulness is wide, which may in part be due to the high diaphragm. Imp: **Aortic dilatation and general enlargement of heart.**	**Hypertrophy of the heart** with aortic insufficiency; chronic nephritis; slight congestive failure.
E. Med. 268172	M 68	No rheumatic infections; denies venereal disease.	210/90	Negative.	Normal rhythm; rate 70; flat T2. Left axis deviation.	Feb., 1925.	R= 6.9; B= 8.8; L=10.0; V=10.9; T=16.9; l=16.5; Chest=24.5.	Heart enlarged transversely, shape of aortic disease. Supracardiac dulness increased, but in oblique view normal. Imp: **Arteriosclerosis.**	**Arteriosclerotic and hypertensive heart disease** with aortic regurgitation; chronic nephritis and uremia.
O. P. D. 528637	M 64	No rheumatic fever, but some indefinite pains years ago. Denies syphilis.	180/90	Negative 1918, 1919, & 1924.		Aug., 1924.	R= 4.5; B=13.0; L=11.0; V= 7.0; T=15.5; l=17.0; Chest=27.0.	Heart shadow enlarged down and to the left, curve of left ventricle being prominent. Aorta is tortuous. Supracardiac dulness increased, but normal in the oblique view. Imp: **Arteriosclerosis.**	**Arteriosclerotic and hypertensive heart disease** with aortic regurgitation. (See Figs. 2-*A* and 2-*B*.)

months previous to the time that one of us saw him they had found a beginning aortic diastolic murmur. The Wassermann reaction at the time was negative; the etiology was, therefore, in doubt. On making an x-ray study of the aorta, a perfectly characteristic syphilitic process was found. Later a strongly positive Wassermann reaction was reported which dispelled any doubt as to the etiology.

Aortic regurgitation in hypertensive and arteriosclerotic heart disease (see Table II). In this series, in contrast to the other groups, there is marked hypertension, the average systolic pressure being 208 mm. In all the cases there was an increase in the supracardiac shadow (?), but with the exception of two cases the aorta was normal in the oblique plane. This is well illustrated in Fig. 2-*A* and Fig. 2-*B*.

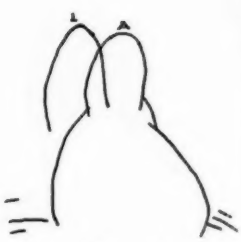

Fig. 3-*A*.

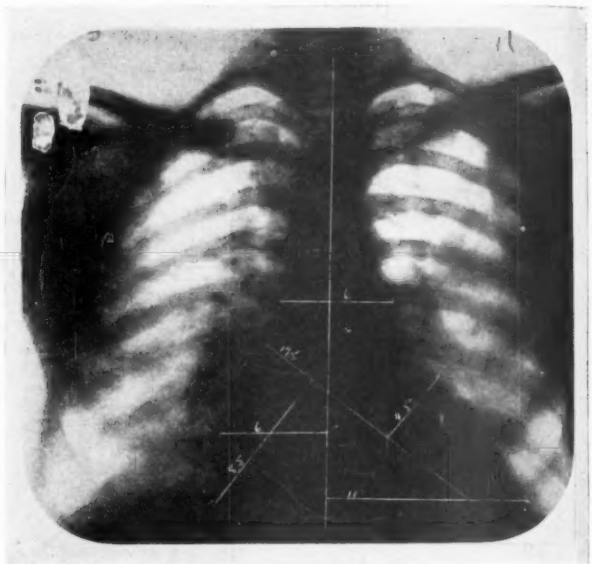

Fig. 3-*B*.

Fig. 3-*A*.—Case E. Med. 255588 (*see* Table III). A case of uncomplicated, aortic regurgitation of rheumatic origin. The heart shadow is enlarged downward and to the left. The supracardiac shadow is not increased. The shadow of the aorta appears normal both in the anteroposterior and in the lateral views. A Wassermann test was strongly positive in this case, and clinically a syphilitic heart lesion was suspected. At autopsy, no evidence of syphilis of the heart or aorta was found. The pathology was confined to the aortic valve, and was characteristic of the rheumatic type.

Fig. 3-*B*.—Teleoroentgenogram. Case E. Med. 255588 from Table III.

In the first exception, W. Med. 254233, there is a general dilatation of the aorta. This may not be unusual in hypertension. The general aortic dilatation is to be differentiated from the rather localized dilatation of the ascending aorta in syphilis where there occurs a cone-shaped shadow. In very rare cases arteriosclerosis has been found to produce this cone-shaped shadow simulating syphilitic aortitis. The second exception, case E. Med. 255245, is probably to be explained upon the hypothesis that the patient previously had had a

TABLE III

FIVE CASES OF UNCOMPLICATED AORTIC REGURGITATION DUE TO RHEUMATIC HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTROCARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
E. Med. 213949	F 32	Tonsillitis severely each winter.		Negative.	Lt. axis deviation. sinoauricular bradycardia.	1917.	R= 4.7; B=10.1; L= 9.8; V= 5.6; T=14.5; I=15.5.	Hypertrophy of left side of heart. No dilatation of aorta. Tracing normal in the oblique view.	**Rheumatic heart disease** with aortic regurgitation.
W. Med. 253850	M 30	Iritis and conjunctivitis in 1915, 1921 and 1922. Gonorrhea in 1914. No "rheumatic" infections. Denies syphilis.	130/78	Negative.		Jan., 1923.	R= 4.1; B=11.3; L= 8.6; V= 6.3; T=12.7; I=15.3; Chest=27.9.	Heart size within normal limits. Supracardiac dulness not increased. Aortic knob a little prominent. **No definite lesion found.**	**Rheumatic heart disease** with slight aortic regurgitation. Syphilis?
E. Med. 265045	F 14	No rheumatic fever, but has chronically infected tonsils.	130/80	Negative.		Sept., 1924.	R= 2.9; B= 9.0; L= 7.0; V= 5.0; T= 9.9; I=11.5; Chest=22.0.	Heart shadow is not enlarged in any direction. **No** increase in supracardiac shadow.	**Rheumatic heart disease** with slight aortic regurgitation. Chr. tonsillitis; subacute nephritis.
E. Med. 264813	F 48	Rheumatism in feet 6 years ago with swelling and pain.	140/80	Negative.	Normal rhythm; rate 70.	Aug., 1924.	R= 4.0; B=10.5; L=10.0; V= 6.5; T=14.0; I=19.0; Chest=26.0.	Heart shadow enlarged downward and to the left. Some increase in supracardiac but no dilatation of the aorta in lateral view. Imp: "**rheumatic.**"	**Rheumatic heart disease** with aortic regurgitation. Acute rheumatic fever.
E. Med. 255588	M 31	"Chancre" in army. Some sore throat. No rheumatism.	130/15	Strongly positive twice.	Right bundle branch block. Rate 100; partial A-V block; P-R =.22". Low T2; V.P.B.	April, 1923.	R= 6.0; B=13.0; L=11.0; V= 6.0; T=17.0; I=19.0; Chest=26.0.	Considerable increase in cardiac shadow transversely, both to the right and left. Supracardiac shadow not increased. **Not syphilitic.**	**Rheumatic heart disease** with aortic regurgitation, subacute bacterial endocarditis and anginal pain.* (See Figs. 3-*A* and 3-*B*.)

*Proved by autopsy—see text.

marked hypertension, again resulting in general aortic dilatation. The patient had slight congestive failure and it has been our observation that with the onset of congestive failure there often is a drop in blood pressure.

Rheumatic aortic regurgitation (see Table III). Aortic regurgitation of rheumatic origin without other valve lesions is thought to be an infrequent condition. The five cases in Table III, however, show that it is not rare for it to be present without the usual mitral lesion. Such a finding in a patient between the age of thirty and forty is rather disturbing, that is, before it is definitely proved that the process is not syphilitic. This is particularly true if a positive Wasser-

Fig. 4-*A*.

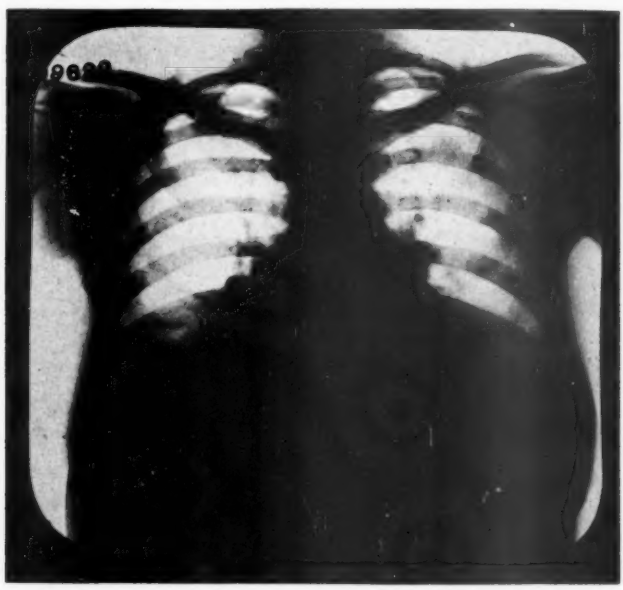

Fig. 4-*B*.

Fig. 4-*A*.—Case from Table IV. A typical case of rheumatic heart disease, with multiple valvular involvement. There is a general enlargement of the heart shadow, without increase in supracardiac dullness. The size of the shadow of the aorta is about the same both in the anteroposteior and in the oblique views. The enlargement of the heart shadow to the right is absent in uncomplicated aortic lesions.

Fig. 4-*B*.—Teleoroentgenogram. Case from Table IV.

mann also be present. Case E. Med. 255588 is such a case; here we have a pulse pressure of 115 mm. and a diastolic pressure of 15 mm., the latter in particular being thought by some to be indicative of syphilitic aortic regurgitation. It so happened that the Wassermann reaction was repeatedly strongly positive in this man; this was enough to swing the clinicians from a previous diagnosis of rheumatic heart disease, despite the fact that the x-ray findings did not indicate syphilis. At autopsy the x-ray was proved correct (see Fig. 3-*A* and Fig. 3-*B*)—a chronic rheumatic and subacute bacterial aortic endo-

TABLE IV

TEN CASES OF AORTIC REGURGITATION WITH MITRAL DISEASE DUE TO RHEUMATIC HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTROCARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
W. Med. 261590	M 14	Rheumatic fever 24 months ago. Stiffness in knees 2½ months ago.	115/40	Negative.	Normal rhythm. Rate 100; low T2; P-R=.2".	Aug., 1924.	R= 5.0; B=12.0; L= 9.9; V= 4.4; T=14.9; l=14.7; Chest=22.0.	Heart shadow much enlarged particularly to the right. Both auricles prominent. No increase in aortic shadow in either view. **"Rheumatic."**	**Rheumatic heart disease** with aortic regurgitation, and mitral stenosis and regurgitation.
C. Med. 262613	M 3	Bronchopneumonia age 3 months. Frequent colds and sore throats. No rheumatism.		Negative.	Partial A-V block; P-R = .28"-.35"; P2=+5 mm.	Apr., 1924.	R= 3.2; B= 7.8; L= 5.5; V= 4.3; T= 8.7; l= 9.2; Chest=15.2.	Heart shadow enlarged down and to the left and across the base. Left ventricle and right auricle prominent. Supracardiac dulness not increased. **Aortic and mitral disease—"rheumatic."**	**Rheumatic heart disease** with aortic regurgitation and mitral stenosis and partial heart block. Syphilis unlikely and congenital heart defects improbable.
W. Med. 263987	M 16	Measles and influenza. Rheumatic fever one year ago.	130/90	Negative.		Aug., 1924.	R= 6.0; B=17.0; L=10.0; V= 8.0; T=16.0; l=13.0; Chest=25.0.	Big left ventricle; prominent auricles. **No enlargement of aorta.**	**Rheumatic heart disease** with aortic regurgitation, and mitral stenosis and regurgitation.
W. Med. 265267	M 15	Scarlet fever several years ago. Slight joint and throat symptoms in recent months.	110/55	He left hospital before Wassermann or electrocardiogram could be done.		Sept., 1924.	R= 5.2; B=10.3; L= 9.0; V= 6.5; T=14.2; l=16.0; Chest=24.6.	Heart shadow increased in size, greatest across the auricles. Big left ventricle. Aorta normal. **"Mitral shaped heart."**	**Rheumatic heart disease** with aortic and mitral regurgitation.
W. Med. 266649	F 26	Rheumatic fever 11 years ago and occasional attacks since.	130/70	Negative.	Sinoauricular bradycardia; rate 50; P-R=.22".	Dec., 1924.	R= 5.7; B=10.1; L= 8.5; V= 7.0; T=14.2; l=15.5; Chest=24.0.	Heart shadow increased in all diameters. Prominent left ventricle. Supracardiac dulness increased, probably due to high position of diaphragm.	**Rheumatic heart disease** with aortic regurgitation, mitral stenosis and regurgitation and paroxysmal auricular flutter.

TABLE IV—CONT'D

TEN CASES OF AORTIC REGURGITATION WITH MITRAL DISEASE DUE TO RHEUMATIC HEART DISEASE

CASE	SEX AGE	PAST HISTORY	B. P.	WASSERMANN	ELECTROCARDIOGRAM	DATE	HEART MEASUREMENTS IN CENTIMETERS* BY X-RAY	X-RAY INTERPRETATION	CLINICAL DIAGNOSIS
W. Med. 265219	F 28	Much rheumatic fever between ages of 12 and 15 years.	130/85	Strongly positive several times.	Auricular fibrillation; ventricular rate 75; diphasic T2.	Jan., 1925.	R= 8.0; B=12.5; L=11.0; V= 5.0; T=19.0; l=17.5; Chest=25.0.	Heart shadow much increased in all diameters. Left ventricle and right auricle prominent. No increase in supracardiac dulness.	**Rheumatic heart disease** with aortic regurgitation, slight aortic stenosis, and mitral stenosis and regurgitation. Auricular fibrillation.
W. Med. 266458	F 31	No "rheumatic" history.	115/70	Negative.	Normal rhythm; rate 85; prominent P2.	Nov., 1924.	R= 3.6; B=11.4; L= 9.3; V= 5.7; T=12.9; l=14.6; Chest=25.6.	Heart shadow prominent in region of left ventricle, and there is a bulge in region of pulmonic artery and left auricle suggesting **"mitral disease."**	**Rheumatic heart disease** with aortic regurgitation, and mitral stenosis and regurgitation. Cardiac irritability.
W. Med. 266260	F 16	Many attacks of rheumatic fever beginning at age of five.	110/45	Negative.		Dec., 1924.	*	Heart shadow large and rather "mitral" in shape. Definite prominence in region of left auricle. ? Enlargement of lef ventricle.	**Rheumatic heart disease** with aortic regurgitation (slight), and mitral regurgitation and ? mitral stenosis.
W. Med. 260514	M 16	Sore throat two years ago. Acute rheumatic fever past few weeks.	142/65	Negative.	Sino-auricular tachycardia. Rate 110; P-R=.22".	Jan., 1924.	R= 3.8; B= 7.3; L= 9.5; V= 7.5; T=13.3; l=13.3; Chest=25.3.	Heart shadow increased particularly to the left. Greatest increase is in region of left auricle. **"Mitral disease."**	**Acute and chronic rheumatic heart disease** with mitral regurgitation and stenosis, and slight aortic regurgitation.
Med. 260656	M 16	Frequent sore throat; bad tonsils; scarlet fever at age of 4; influenza 1918.	190/0	Negative.	Sinus arrhythmia; rate 110; Slt. left axis Inverted deviation. T2 and T3.	Jan., 1924.	R= 4.3; B=10.4; L= 8.8; V= 5.5; T=13.1; l=14.8; Chest=22.5.	Enlargement of the heart downward and to the left with prominence of left ventricle and slight prominence of left auricle. Great vessels normal. **"Rheumatic heart."**	**Rheumatic heart disease** with marked aortic regurgitation and moderate mitral stenosis.

*Not a 7-foot plate—no measurements made.

carditis was found. This case moreover is of great interest from the standpoint of the mechanism of angina pectoris. No disease of the aorta or coronary arteries was present, but there was a vegetation on one of the aortic valves large enough to swing over and occlude the left coronary artery thus explaining the pain. Case W. Med. 253850 had a past history highly suggestive of syphilis though he did not have a positive Wassermann. However, the x-ray served definitely to point out that the process was nonsyphilitic.

Rheumatic aortic regurgitation plus mitral involvement (see Table IV). It is notable that in these cases the x-ray department easily made the diagnosis of rheumatic heart disease and in all instances agreed with the clinical findings (see Fig. 4-*A* and Fig. 4-*B*). There are two cases that are well worth discussion. The first, W. Med. 265219, was a female aged twenty-eight years with a positive Wassermann reaction and aortic diastolic and mitral mid-diastolic murmurs. Although it was definitely felt that her cardiac lesions were of rheumatic origin it was of no little aid to know by the x-ray that there was no evidence of increase in size of the aorta. One must remember that a syphilitic process may also be present with rheumatic involvement. In our observations the x-ray has not shown any localized change in the aortic shadow in rheumatic aortic regurgitation, despite the fact that definite lesions have been found by Pappenheimer and Von Glahn[11] histologically, and in rare cases by Deusch[12] by x-ray. The second case, Med. 260656, again shows the fallacy of considering too strongly a low diastolic pressure as indicative of syphilitic process. In this instance it was so low as to be called zero.

SUMMARY

1. Thirty-four cases of aortic regurgitation of various types have been studied by us with particular reference to the x-ray findings.

2. We have found that the x-ray is of distinct help in differentiating between aortic regurgitation of syphilitic, rheumatic, arteriosclerotic, and hypertensive origin. The chief points of differentiation are discussed. Our method of study of the heart and aorta by the x-ray is presented.

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EXPERIMENTAL HEART DISEASE*

I. Methods of Dividing Hearts; with Sectional and Proportional Weights and Ratios for Two Hundred Normal Dogs' Hearts

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INTRODUCTION

HEART muscle changes present many important problems of clinical as well as fundamental or theoretical interest. The study[1, 2] of a large series of human hearts in which the antemortem electrocardiographic signs and the postmortem sectional and proportional heart weights and ratios were frequently not in accord, when the hearts were only slightly or moderately enlarged, prompted the investigations that are to be reported in this and subsequent papers.

Advances in the knowledge of the fundamental factors in heart disease must rest in some measure at least upon carefully controlled experimental cardiological studies. The reliability of deductions from the results of investigations is directly proportional to the standardization of methods and the adequacy of control series for the normal and the experimental animals. To this end I shall discuss in detail the methods used and report in detail my checked control data for two hundred normal dogs. Extensive tables will be included giving the sectional and proportional weights and ratios, the mean averages, the normal limits and the statistical functions for the various segments of the dog's heart.

The values for the sections obtained by both the standard methods, the author's, midseptal line and anteroporterior angle bisecting method, and Lewis', conus tendon and tangential septum cuts method, are recorded. Dogs were chosen as the most suitable of the ordinary experimental animals for this type of work, because the hearts are of sufficient size to be divided and weighed with a fair degree of accuracy.

Although primarily undertaken to determine the effect of preponderant left ventricular hypertrophy accompanying experimentally produced aortic insufficiency, upon the electrocardiogram of the dog, the research rapidly broadened out to touch upon many of the fundamental questions of the cardiac and especially the myocardial response to stress, strain, traumatic and toxic injury and infection.

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METHODS

Inasmuch as some studies using somewhat different and, in our opinion, less accurate methods, have been made, it seems advisable to discuss at some length the methods of sectioning human as well as dogs' hearts. The preparation and the fixation of the hearts for sectioning are also given in detail.

Müller's[3] traditional method was carried out on fresh soft heart muscle according to directions that are but briefly stated. These factors tend to introduce error, as Lewis pointed out, and make the establishment of normal standard ratios difficult. In the inadequate

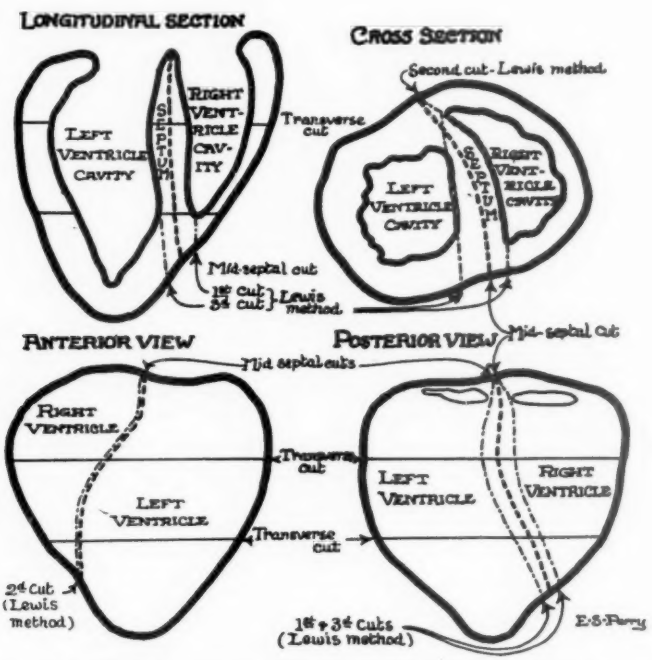

Fig. 1.—Outline drawings representing the longitudinal and cross sections and the anterior and posterior views of a heart, with the locations of the midseptal cut of the author's method indicated by a heavy dash line, and the three cuts of Lewis' method indicated by lighter dash dot lines.

description of the method the author mentions only the landmarks of the superficial cuts used in the separation of the fresh ventricles. A cut is carried along the interventricular groove anteriorly and posteriorly. Then, in order to separate the septum which is not so clearly marked off from the left ventricle as it is from the right, the muscle is cut radially along the incision made for the removal of the right ventricle. Wolfer[4] modified the method by making a superficial incision in the interventricular sulcus and carrying out the separation by blunt dissection, which removed the free walls of the right ventricle, leaving the septum with the left

ventricle which thus remained a complete unit with a closed cavity. This modification has, however, won no advocates.

Lewis'[75] *Method* requires careful preparation of the specimen and fixation before the dissection is undertaken. The results are more uniform,

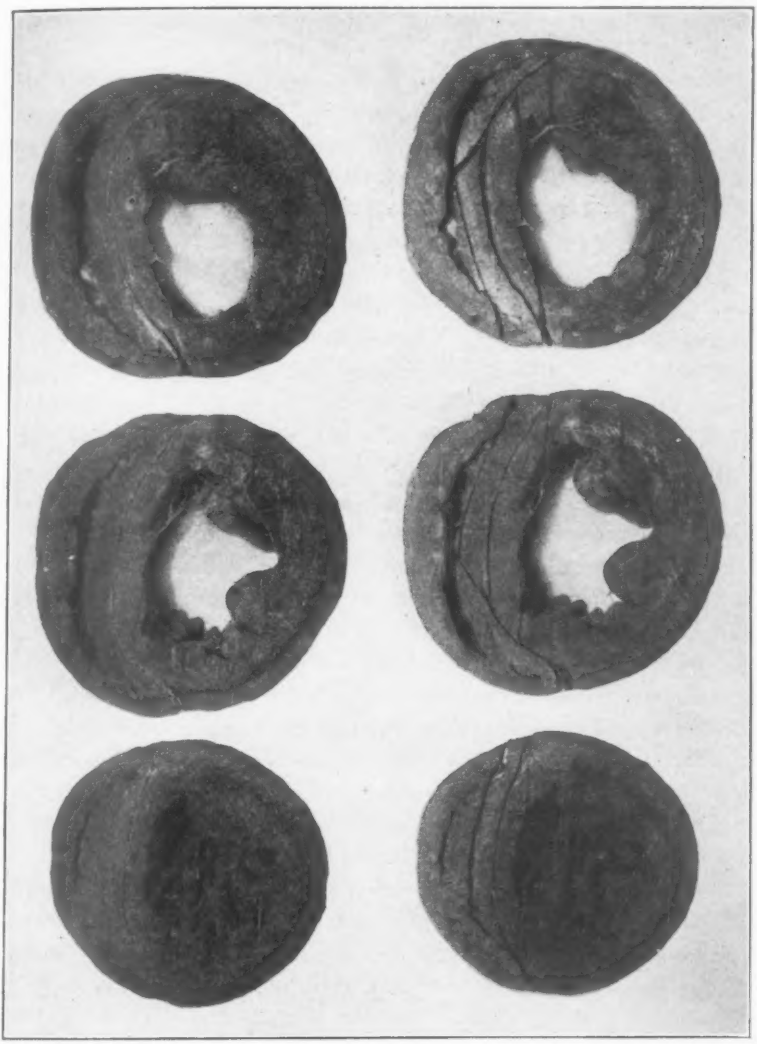

Fig. 2.—Photographs of the cross sections of the heart of dog No. 59, showing on the left side the ventricles separated by the author's method and on the right the same sections after the cuts of the Lewis' method had been made. This figure shows how easily both methods of dissection can be used in the same heart.

reliable and standard. Lewis' descriptions are very concise and will consequently bear repeating.

The cavities of the fresh heart, with the parietal pericardium removed and the vessels cut short, are washed free of blood and clots.

The water is allowed to drain off and the specimen is weighed. The orifices are all closed by tying or clamping off all of the great vessels. The heart cavities are then distended by the injection of 10 per cent formalin solution into them with a syringe and needle. The distended heart is then immersed in 10 per cent formalin for four to seven days, according to its size. The weight of the specimen increases during this stage. The orifices of the fixed heart are then opened, the formalin is drained off, and the specimen is washed in running water for one or two days. The fixed heart is then placed in a 70 per cent alcohol solution, in which there is a loss of weight, for six or seven days or until the weight is back to the original figure. The epicardium, subepicardial fat and the coronary vessels are removed by careful dissection. The valves, chorda tendinae and any remaining clots are removed. The intact, clean ventricular muscle is then weighed.

Lewis' Method for the Separation of the Ventricles (see Figs. 1 and 2) is carried out as follows: Large hearts are bisected horizontally and the cuts in the upper portion are subsequently made in the lower portion. The *first cut* runs parallel to the septum, beginning at its junction with the right wall above and posteriorly taking as much of the right wall as is necessary to make the cut tangential to the septum where it joins the wall, and at the same time separating from the septum all loose ventricular trabeculae and the papillary muscle. The *second cut* is along the straight white fibrous line (conus tendon) which unites the pulmonary conus arteriosus (infundibulum) to the septum and the left ventricle anteriorly, and is carried downward generously enough to separate all loose ventricular trabeculae from the septum and retain the infundibulum as a complete muscular tube. On the anterior surface of the heart the cut lies in the interventricular sulcus throughout its course until it joins the posterior cut. These two cuts prolonged to the apex leave no deep sulci upon the septal wall. The *third cut* is parallel to the first at the junction of the left wall with the septum above and posteriorly, in a line tangential to the cavity of the left ventricle at the center of the septum and passing into the second cut in front approximately at the center of the conus tendon. This cut continued downward separates the left ventricle from the septum as a chamber with a vertical opening 1 to 2 cm. across because of the curvature of the septum toward the right.

The three segments are placed in water and weighed separately every day until the weights are constant from day to day. There is a final gain in weight in this stage, usually sufficient to restore the muscle to its original weight with sufficient precision. The A-V node region may be prepared with the septum, an equal amount of auricular wall being weighed and the amount subtracted from the septal weight.

The Author's Method was originated to meet the desires for a less arbitrary and more precise, as well as more natural, method of separa-

tion of the ventricles. Modifications in the methods of preparation also had to be evolved to secure the desired concessions from the prosector, who is generally desirous of seeing the valves and the endocardial surfaces in the fresh state during the autopsy.

The parietal pericardium, if still attached, is removed. The pad of fat at the root of the great vessels is removed. The aorta and pulmonary artery are cut off at the level of the tops of the valve commissures and the veins are removed flush with the auricular wall. The auricles are opened by cuts joining the venous orifices and extending into the auricular appendages. The fat in the A-V groove is then about equally divided between auricles and ventricles, while the coronary arteries are palpated and pressed down and left intact on the ventricular muscle. The knife is passed through the auricular wall from the incision in the fat of the A-V sulcus to the valve ring at which the auricular muscle is attached. This attachment is severed all around except when the A-V node, bundle and branches are to be preserved intact for special study, under which circumstances the cuts separating the interauricular septum from the interventricular septum are carried up from the valve ring attachment to the level of the top of the coronary sinus orifice in the right auricle. A section of the interauricular septum equal to that left attached to the top of the interventricular septum is weighed and its weight subtracted from the ventricular weight and septal weight.

The auricles may be divided by splitting the septum, and weighed individually. Fluid blood or any remaining clots are then expressed from the ventricles and the weight of the fresh and uncleaned muscle determined. All the valve leaflets or cusps, chorda tendinae, and the ventricular endocardium are well exposed. The valve segments may be floated up and the rough hydrostatic test of function may be performed by running water into the ventricles. The ventricular capacities may be measured with water and with mercury at this point. The mercury distended ventricles are suspended in 10 per cent formalin from hat pins thrust through the base. The ventricles may, however, be fixed undistended. Further dissection may be carried out in the fresh state or one may postpone the separation until after fixation is complete. When possible it is best to fix the ventricular muscle completely before undertaking the separation of the ventricles.

The coronary arteries are then slit open beginning at their orifices in the aortic sinuses and following the vessels around the A-V groove and down the anterior and the posterior interventricular sulci. The whole top plane, including all the valves and the roots of the aorta and the pulmonary artery, may be removed in toto and preserved to be subsequently fitted on a plaster model of the ventricles. To accomplish this a cut is made just through the epicardium in the greatest circumference. The epicardium, vessels and fat are dissected back

over the conus and the rounded bases of the ventricles to the valve rings and the roots of the great vessels. The chordae tendinae are all severed at the apices of the papillary muscles. With the epicardium, vessels, fat and basal tissues retracted to the A-V valve rings, the latter are cut through and the mitral and tricuspid valves are freed. The basal tissues with the A-V valves can then be retracted sufficiently to expose the junction of the semilunar cusps and the endocardium. This junction is then used as a line of separation and the roots of the aortae are dissected free from below up and the whole base with all valves can be lifted off the ventricular muscle. The remaining epicardium, fat and coronary vessels are all removed. The cleaned ventricular muscle fresh or fixed is weighed and the capacities of the cavities estimated with mercury and recorded.

The fixation procedure that we have employed consists in immersion in 10 per cent formalin for ten to fifteen days. This simplified method of fixation has many advantages, chief among which is the ease with which the ventricular muscle can be brought back to its autopsy weight, as well as being completely fixed. In daily weighings of a large series we noted an initial gain of a few to several grams in the ventricular weight during the first two to four days, and then a gradual fall to the autopsy weight in six to ten days. From this point on there is very little change for several days, and the transfer of the specimen to water maintains the weight, while a continuation of the formalin stage causes a gradual but irreplaceable loss of weight. Occasionally the gain is slight or *nil* and there may even be a slight loss. Minor changes of this sort are, however, not of great significance, since the changes are proportional and do not affect the L/R ratio. In a goodly number of instances we have observed that an L/R ratio at the time of a gain in weight differed very little or not at all from that calculated after there had been considerable loss in weight. It is, however, desirable and we have always made it a point to work with specimens that have been restored to the original fresh or autopsy weight in order to have more accurate proportional ratios.

The Author's Method for the Separation of the Ventricles (see Figs. 1 and 2) consists in dividing the ventricular muscle mass in the plane of the midseptal line. The latter line is an anatomical landmark formed by the intersection of the scroll muscle layers from the two ventricles. This fact, in my opinion, makes the method less arbitrary, less subject to error and less influenced by the degree of distention of the ventricular cavities.

The cleaned and fixed ventricular muscle mass is cut horizontally; that is, at right angles to the long axis, into a series of sections of one to two centimeters in thickness. A quick cut with a sharp, thin brain knife will bring out the midseptal line most conspicuously.

Each segment is then divided in the plane of the midseptal line which is apparent on the cut surfaces. Anteriorly and posteriorly where the lines form to go to each ventricle, the cuts are made in a plane bisecting the angle between the forks which bring them into the plane of the interventricular sulci. In the case of the upper segment, the cut is carried along the conus tendon through the middle of the top of the interventricular septum, thence directly backward grossly bisecting the wide angle to the posterior sulcus. The incision on the superior surface and that along the midseptal line on the cut or inferior surface are joined by the knife blade, thus completing the division in the plane of the midseptal line. In the case of the apex segment there is a midseptal line and angles to be followed on the superior surface only and in order to complete the separation in the plane of this line, the interventricular sulci marked by the terminal branches of the anterior and posterior descending coronary vessels are followed as landmarks. The plane of the midseptal line is usually perpendicular to that of the superior surface of the apex segment and along the line on this surface.

In the separation of the ventricles by this method the septal muscle is distributed between the two ventricles and consequently cannot be weighed separately. However, after a series of weighings at intervals, the segments may be further sectioned according to the method of Lewis (see Figs. 1 and 2). The latter procedure can be applied with ease and accuracy after the division by our method. Our midseptal line method may be applied to hearts in the fresh state, but more accurate, more reliable and more satisfactory results are obtained with the formalin-fixed ventricular muscle.

PREVIOUS NORMAL SERIES AS CONTROL DATA

The traditional method of Müller, which is the most inaccurate of the standard methods, is practically the only one that has been employed in the establishing of normal control series for experimental animals. Hasenfeld and Romberg[6] reported average, maximum and minimum values for the heart weight, body weight and the right ventricular weight and the left ventricular weight ratios for a series of thirty-two normal rabbits. Great individual variations were noted and I believe this due to the fact that the rabbit's heart is too small to be divided and weighed with any degree of accuracy whatsoever.

In the case of dogs, which I consider the only satisfactory animal for studies of this type, there is even a greater paucity of data available. The heart weight body weight (H.W./B.W.) ratio alone for normal dogs had been reported to average 0.00970 by Heinz[7] in Germany, while Joseph[8] in the United States had found the average ratio to be 0.00740. This difference was considered to be possibly due to the difference in the breed of dogs used. Hugh A. Stewart's[9]

TABLE I—200 NORMAL CONTROLS

	WEIGHTS AND L/R RATIOS												GENERAL SEGMENTAL RATIOS								
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
						AUTHOR'S METHOD			LEWIS' METHOD												
	BODY WT. IN KG.	FRESH TOTAL HEART WT. IN GMS.	FRESH AUR. WT.	FRESH VENT. WT.	CLEAN AND FIXED VENT. WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	SEPTUM WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	RATIO TOTAL HT. WT. BD. WT.	FRESH AUR. WT. BD. WT.	FRESH VENT. WT. BD. WT.	CLEAN AND FIXED VENT. WT. BD. WT.	H. L. VENT. BD. WT.	H. R. VENT. BD. WT.	L. SEPTUM BD. WT.	L. L. VENT. BD. WT.	L. R. VENT. BD. WT.
	15.1	122.75	18.75	104.	87.	50.	37.	1.350	14.	42.	31.	1.355	.00813	.00124	.00690	.00575	.00332	.00245	.00093	.00278	.00205
	15.1	132.25	17.5	115.	88.4	53.3	35.1	1.520	15.7	44.7	31.5	1.417	.00877	.00116	.00762	.00585	.00353	.00232	.00104	.00296	.00208
	18.5	159.5	30.5	129.	112.	60.	52.	1.153	22.2	50.2	41.	1.225	.00863	.00165	.00698	.00606	.00324	.00286	.00120	.00272	.00222
	6.6	60.	7.5	52.5	46.3	26.5	19.8	1.338	8.5	22.2	16.4	1.352	.00910	.00114	.00796	.00700	.00402	.00300	.00129	.00336	.00249
	8.5	74.	10.	64.	57.8	32.5	25.3	1.285	10.	26.5	21.5	1.232	.00870	.00118	.00753	.00680	.00382	.00298	.00118	.00312	.00253
	9.5	85.5	10.	75.5	67.2	36.7	30.5	1.200	13.	29.2	25.4	1.150	.00900	.00105	.00795	.00708	.00386	.00321	.00137	.00308	.00268
	9.	56.75	8.75	48.	41.3	25.3	16.	1.580	7.75	21.	13.3	1.580	.00632	.00097	.00534	.00460	.00282	.00178	.00086	.00234	.00148
	11.6	93.5	10.5	83.	70.6	42.3	28.3	1.494	11.8	36.7	23.	1.595	.00807	.00091	.00715	.00610	.00365	.00244	.00102	.00316	.00198
	8.7	74.	10.5	63.5	50.5	28.	22.5	1.244	9.5	24.	18.75	1.282	.00852	.00121	.00730	.00581	.00322	.00259	.00108	.00276	.00216
	6.6	50.	10.	40.	35.75	20.5	15.25	1.345	6.5	17.5	12.	1.458	.00757	.00152	.00606	.00540	.00311	.00231	.00099	.00266	.00182
	6.8	52.	8.5	43.5	35.	20.7	14.3	1.448	6.25	16.75	12.25	1.368	.00765	.00125	.00640	.00515	.00305	.00210	.00092	.00247	.00180
	11.4	78.5	12.	66.5	57.25	33.	24.25	1.348	10.5	27.	20.5	1.316	.00689	.00105	.00584	.00502	.00290	.00213	.00092	.00237	.00180
	11.4	86.5	12.	74.5	59.9	34.3	25.6	1.340	10.5	29.7	21.	1.415	.00759	.00105	.00654	.00525	.00301	.00224	.00092	.00260	.00184
	7.3	67.5	9.5	58.	49.5	29.	20.5	1.413	9.5	25.	16.8	1.488	.00925	.00130	.00795	.00678	.00398	.00281	.00130	.00343	.00230
	13.25	90.	12.5	77.5	70.25	43.75	26.5	1.650	11.5	37.25	21.3	1.750	.00680	.00094	.00584	.00530	.00330	.00200	.00087	.00282	.00161
	12.35	110.5	13.	97.5	88.	50.5	37.5	1.348	14.	43.5	30.5	1.425	.00895	.00105	.00788	.00712	.00408	.00304	.00113	.00352	.00247
	10.	76.	9.5	66.5	58.3	36.	22.3	1.615	11.	29.5	18.25	1.617	.00760	.00095	.00665	.00583	.00360	.00223.	00110	.00295	.00183
	5.4	48.	7.5	40.5	36.	20.	16.	1.250	6.3	16.5	13.75	1.200	.00890	.00139	.00750	.00667	.00370	.00296	.00117	.00306	.00255
	8.25	77.5	10.5	67.	61.5	36.	25.5	1.412	11.5	30.5	20.5	1.488	.00940	.00127	.00813	.00746	.00437	.00310	.00139	.00370	.00249
	6.7	56.5	7.5	49.	42.	24.5	17.5	1.400	8.0	21.5	15.	1.433	.00844	.00112	.00732	.00627	.00366	.00262	.00119	.00321	.00224
	12.35	99.	15.	84.	75.2	42.7	32.5	1.310	12.5	36.	28.	1.286	.00800	.00121	.00680	.00610	.00346	.00263	.00101	.00292	.00227
	10.6	88.	9.5	78.5	68.5	38.25	30.75	1.245	12.4	31.7	26.25	1.208	.00830	.00089	.00740	.00647	.00365	.00290	.00117	.00299	.00248
	8.	50.	8.5	41.5	39.7	23.1	16.6	1.392	6.25	19.75	15.	1.316	.00625	.00106	.00518	.00497	.00289	.00208	.00078	.00247	.00188
	8.8	64.	9.	55.	49.5	29.	20.5	1.413	8.25	25.	18.	1.388	.00727	.00102	.00625	.00563	.00330	.00234	.00094	.00284	.00205

TABLE I—CONT'D

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
14.85	105.5	14.5	90.5	79.5	48.	31.5	1.525	15.25	44.1	25.	1.764	.00711	.00098	.00609	.00535	.00334	.00212	.00103	.00297	.00168
12.1	78.5	12.	66.5	60.25	34.	26.25	1.292	10.6	27.4	21.4	1.280	.00650	.00099	.00550	.00498	.00281	.00217	.00087	.00226	.00177
8.	70.	8.	63.	52.7	29.8	22.9	1.300	8.6	26.	19.1	1.360	.00875	.00100	.00788	.00660	.00372	.00287	.00107	.00326	.00239
8.5	74.5	6.5	68.	64.5	35.	29.5	1.190	12.4	28.1	24.	1.170	.00877	.00076	.00800	.00760	.00412	.00348	.00146	.00330	.00283
7.8	72.5	12.	60.5	54.7	34.2	20.5	1.670	11.1	27.9	18.5	1.510	.00930	.00154	.00776	.00702	.00438	.00263	.00142	.00358	.00237
21.25	127.25	18.5	108.75	100.5	58.5	42.	1.392	16.5	49.75	33.4	1.490	.00600	.00087	.00512	.00473	.00275	.00198	.00078	.00234	.00157
13.75	106.	13.5	92.5	84.4	50.1	34.3	1.460	15.	42.	30.	1.400	.00771	.00098	.00674	.00613	.00372	.00249	.00109	.00306	.00218
8.	67.5	8.	59.5	51.5	31.5	20.	1.575	10.2	25.7	16.	1.609	.00845	.00100	.00744	.00645	.00394	.00250	.00128	.00322	.00200
17.4	112.	17.	95.	86.7	49.	37.7	1.300	15.	41.	27.	1.518	.00644	.00098	.00546	.00498	.00282	.00216	.00086	.00236	.00155
11.5	85.	12.5	72.5	61.2	33.5	27.7	1.210	10.5	27.6	22.7	1.214	.00738	.00109	.00630	.00532	.00292	.00241	.00091	.00240	.00197
12.3	88.5	9.5	78.	67.75	39.25	28.5	1.378	11.	32.5	23.75	1.370	.00720	.00077	.00634	.00550	.00319	.00232	.00089	.00264	.00193
5.75	49.5	6.75	41.5	35.5	21.5	14.	1.535	6.5	18.25	11.75	1.552	.00862	.00117	.00723	.00620	.00374	.00244	.00113	.00318	.00204
17.3	112.5	11.5	101.5	84.8	48.	36.8	1.305	14.6	40.	29.7	1.345	.00650	.00067	.00587	.00490	.00278	.00213	.00085	.00231	.00172
7.75	65.5	7.5	58.	58.5	31.5	27.	1.170	10.8	25.8	21.2	1.216	.00845	.00097	.00750	.00755	.00407	.00349	.00139	.00333	.00274
15.3	116.	15.5	100.5	97.5	56.	41.5	1.348	18.	44.5	34.5	1.290	.00758	.00101	.00657	.00636	.00366	.00271	.00118	.00291	.00226
9.	75.5	8.5	67.5	58.5	34.	24.5	1.389	10.2	29.	20.2	1.435	.00840	.00094	.00750	.00650	.00378	.00272	.00113	.00322	.00227
12.4	108.	12.	96.	87.	47.5	39.5	1.202	15.	39.7	32.5	1.220	.00872	.00097	.00774	.00580	.00334	.00246	.00109	.00208	.00187
6.3	45.	5.	40.	36.5	21.	15.5	1.355	6.9	17.6	11.8	1.490	.00715	.00079	.00635	.00580	.00334	.00246	.00109	.00280	.00187
14.35	115.	11.5	103.5	89.2	51.	38.2	1.335	14.5	43.8	30.5	1.435	.00803	.00080	.00722	.00622	.00356	.00268	.00101	.00305	.00212
17.4	123.	12.5	110.5	98.5	58.8	40.	1.468	17.	50.5	30.7	1.644	.00707	.00072	.00635	.00567	.00338	.00230	.00098	.00290	.00176
11.5	96.	9.5	86.5	79.8	46.8	33.	1.420	13.5	39.5	25.5	1.548	.00835	.00083	.00752	.00695	.00407	.00287	.00109	.00343	.00222
12.	84.	10.5	73.5	68.5	40.5	28.	1.446	11.6	34.8	21.7	1.604	.00700	.00088	.00613	.00570	.00337	.00233	.00097	.00290	.00181
12.	91.	9.	82.	71.2	41.7	29.5	1.414	13.	33.6	24.	1.400	.00758	.00075	.00684	.00594	.00348	.00246	.00108	.00280	.00200
12.25	86.	8.5	77.5	68.8	39.8	29.	1.372	14.4	33.	22.2	1.480	.00702	.00069	.00633	.00562	.00325	.00237	.00118	.00269	.00181
6.5	40.5	5.5	35.5	32.5	19.5	13.	1.500	6.	15.6	10.3	1.516	.00624	.00085	.00546	.00500	.00300	.00200	.00092	.00240	.00519
15.	92.	9.3	82.	76.5	44.5	31.5	1.412	15.0	35.0	24.	1.458	.00614.	00062	.00546	.00510	.00296	.00210	.00100	.00234	.00160
8.9	61.	6.	55.	52.5	30.	21.5	1.396	8.8	26.2	17.5	1.498	.00686	.00067	.00618	.00590	.00337	.00242	.00099	.00294	.00197
6.75	65.8	7.	58.8	56.5	31.5	23.	1.370	10.	26.2	17.5	1.498	.00975	.00104	.00872	.00837	.00467	.00341	.00148	.00388	.00260
7.15	48.6	5.6	43.	39.5	23.	16.	1.438	8.	19.5	11.5	1.698	.00682	.00078	.00602	.00553	.00322	.00224	.00112	.00273	.00161
9.5	79.5	9.5	70.	67.	38.	28.5	1.332	13.5	30.6	22.5	1.360	.00837	.00100	.00737	.00705	.00400	.00300	.00142	.00322	.00237
7.55	64.	7.5	56.	48.5	27.5	21.	1.310	8.5	23.5	17.2	1.368	.00847	.00099	.00742	.00643	.00364	.00278	.00113	.00312	.00227
11.3	100.4	16.9	83.5	80.5	46.5	32.3	1.440	14.	39.5	25.	1.580	.00890	.00149	.00738	.00712	.00411	.00288	.00124	.00350	.00221
12.6	107.5	18.1	89.4	85.8	45.2	38.5	1.174	14.3	36.7	30.5	1.200	.00854	.00144	.00710	.00682	.00358	.00306	.00113	.00291	.00242

TABLE I—CONT'D

	WEIGHTS AND L/R RATIOS												GENERAL SEGMENTAL RATIOS								
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
						AUTHOR'S METHOD				LEWIS' METHOD											
	BODY WT. IN KG.	FRESH TOTAL HEART WT. IN GMS.	FRESH AUR. WT.	FRESH VENT. WT.	CLEAN AND FIXED VENT. WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	SEPTUM WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	RATIO TOTAL HT. WT. BD. WT.	FRESH AUR. WT. BD. WT.	FRESH VENT. WT. BD. WT.	CLEAN AND FIXED VENT. WT. BD. WT.	H. L. VENT. BD. WT.	H. R. VENT. BD. WT.	L. SEPTUM BD. WT.	L. L. VENT. BD. WT.	L. R. VENT. BD. WT.
	10.	87.5	10.	77.5	73.2	40.2	33.	**1.214**	13.5	33.	25.	**1.318**	.00875	.00100	.00775	.00732	.00402	.00330	.00135	.00330	.00250
	7.5	68.	7.	61.	58.8	32.	26.8	**1.194**	11.5	25.5	20.5	**1.244**	.00907	.00093	.00814	.00785	.00427	.00358	.00153	.00340	.00274
	7.75	77.	7.5	69.5	67.5	36.5	31.	**1.178**	13.	30.	24.8	**1.210**	.00994	.00097	.00896	.00870	.00472	.00400	.00168	.00388	.00321
	10.4	72.5	8.	64.5	62.	36.5	25.5	**1.430**	13.5	31.	18.	**1.721**	.00697	.00077	.00620	.00595	.00351	.00245	.00130	.00298	.00173
	18.15	140.	15.	125.	117.5	68.5	48.	**1.428**	21.5	57.5	36.5	**1.574**	.00772	.00083	.00688	.00647	.00378	.00264	.00118	.00317	.00205
	3.5	32.5	3.5	29.5	27.5	16.3	11.2	**1.455**	5.	13.5	8.5	**1.590**	.00930	.00100	.00844	.00786	.00466	.00320	.00143	.00386	.00243
	14.2	130.	12.5	118.5	95.	64.5	41.5	**1.553**	18.5	54.5	32.	**1.700**	.00915	.00088	.00835	.00668	.00454	.00292	.00130	.00384	.00226
	5.4	42.5	4.5	38.	35.7	20.5	15.2	**1.350**	7.5	16.	11.	**1.454**	.00788	.00083	.00705	.00662	.00380	.00282	.00139	.00296	.00240
	5.5	45.7	4.7	41.	38.5	22.	16.5	**1.333**	7.	18.	12.	**1.510**	.00832	.00085	.00746	.00700	.00400	.00300	.00127	.00328	.00218
	4.	30.	3.5	26.5	24.7	14.9	9.8	**1.522**	5.2	12.	7.5	**1.600**	.00750	.00087	.00663	.00617	.00373	.00245	.00130	.00300	.00187
	1.3	10.	1.5	8.5	8.2	5.2	3.	**1.735**	1.8	4.3	2.5	**1.720**	.00770	.00115	.00654	.00630	.00400	.00231	.00139	.00331	.00192
	11.7	90.	11.2	78.8	68.	38.5	29.5	**1.310**	12.5	32.	23.5	**1.362**	.00770	.00096	.00674	.00582	.00330	.00252	.00107	.00274	.00201
	12.8	112.	15.	97.	87.5	50.	37.5	**1.332**	17.	40.	28.5	**1.402**	.00876	.00117	.00756	.00684	.00394	.00293	.00133	.00312	.00222
	9.25	78.5	10.	68.5	61.	36.	25.	**1.440**	10.5	30.	20.	**1.500**	.00850	.00108	.00740	.00660	.00390	.00271	.00114	.00324	.00216
	10.	90.	10.	80.	72.	41.	31.	**1.322**	15.	31.	23.	**1.348**	.00900	.00100	.00800	.00720	.00410	.00310	.00150	.00310	.00230
	8.3	61.	7.	54.	48.	30.	18.	**1.667**	9.8	23.2	14.	**1.655**	.00736	.00084	.00650	.00578	.00362	.00217	.00118	.00280	.00169
	10.	71.	7.	64.	58.	35.	23.	**1.520**	11.	28.	18.	**1.555**	.00710	.00070	.00640	.00580	.00350	.00230	.00110	.00280	.00180
	13.	96.5	9.	87.5	78.	46.5	31.5	**1.475**	16.	36.5	24.5	**1.490**	.00742	.00069	.00672	.00600	.00358	.00242	.00123	.00281	.00188
	12.	82.	12.	70.	62.	35.5	26.5	**1.340**	11.5	29.5	21.	**1.404**	.00684	.00100	.00584	.00516	.00296	.00221	.00096	.00246	.00175
Averages for 80 Females---	12.5	122.	12.	110.	100.	61.5	38.5	**1.600**	20.	48.5	29.5	**1.646**	.00976	.00096	.00880	.00800	.00493	.00308	.00160	.00388	.00236
	10.5	78.	7.5	71.5	67.5	40.	27.5	**1.454**	13.5	31.5	21.	**1.500**	.00743	.00072	.00681	.00643	.00381	.00262	.00129	.00300	.00200
	9.4	60.5	6.0	55.	50.	31.	19.	**1.630**	11.5	23.5	15.	**1.570**	.00644	.00064	.00586	.00532	.00330	.00202	.00122	.00250	.00160
	17.5	122.	15.5	106.5	98.5	54.	44.5	**1.210**	18.5	45.	35.	**1.290**	.00699	.00089	.00610	.00563	.00308	.00254	.00106	.00257	.00200
	10.5	*82.07*	*10.3*	*71.78*	*64.29*	*37.23*	*27.09*	**1.390**	*11.71*	*30.91*	*21.69*	**1.441**	*.00792*	*.00099*	*.00693*	*.00623*	*.00361*	*.00262*	*.00115*	*.00299*	*.00210*

TABLE I—CONT'D

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
15.6	136.5	17.5	119.	98.5	60.	38.5	1.558	15.7	51.3	34.3	1.495	.00876	.00112	.00763	.00625	.00384	.00246	.00101	.00329	.00220
20.1	155.	18.5	137.	108.	66.	42.	1.570	17.	57.2	36.2	1.580	.00786	.00092	.00632	.00532	.00328	.00209	.00085	.00284	.00180
10.8	99.	14.	85.	70.5	38.5	31.5	1.222	12.5	31.5	27.4	1.150	.00917	.00130	.00787	.00653	.00356	.00292	.00116	.00292	.00254
18.	166.5	24.	142.5	122.2	74.5	47.7	1.562	22.8	61.5	39.7	1.549	.00925	.00133	.00792	.00680	.00414	.00265	.00127	.00342	.00220
16.25	107.	17.	90.	79.5	43.5	36.	1.210	17.5	33.3	27.7	1.200	.00660	.00105	.00554	.00489	.00268	.00222	.00108	.00205	.00171
11.45	104.5	12.5	92.	83.5	47.	36.5	1.288	15.	38.5	30.	1.282	.00914	.00109	.00803	.00730	.00411	.00318	.00131	.00336	.00262
8.65	76.	10.5	65.5	58.25	34.	24.25	1.400	12.	28.	20.	1.400	.00878	.00121	.00758	.00675	.00394	.00281	.00139	.00324	.00232
8.4	64.5	8.	56.5	50.4	29.2	21.2	1.378	10.	24.2	17.	1.425	.00768	.00095	.00674	.00600	.00348	.00252	.00119	.00288	.00201
8.5	61.5	8.5	53.	47.	25.5	21.1	1.210	9.	21.2	17.	1.248	.00724	.00100	.00624	.00553	.00300	.00249	.00106	.00250	.00200
18.	112.5	15.5	96.5	85.	49.2	35.8	1.374	15.	40.	30.	1.332	.00625	.00086	.00536	.00473	.00273	.00199	.00083	.00222	.00167
16.3	151.5	24.	127.5	110.	62.	48.	1.290	16.	53.8	39.5	1.362	.00955	.00147	.00784	.00676	.00380	.00295	.00098	.00330	.00242
23.7	155.	20.	135.	115.5	68.	47.5	1.432	23.	56.	37.2	1.505	.00655	.00084	.00570	.00488	.00287	.00200	.00097	.00236	.00157
5.8	49.	5.	44.	40.	23.5	16.5	1.425	7.5	19.8	13.8	1.435	.00846	.00086	.00760	.00690	.00406	.00285	.00129	.00342	.00238
6.4	61.	10.	50.	46.5	26.	21.5	1.208	9.25	20.8	17.3	1.200	.00950	.00156	.00782	.00726	.00407	.00336	.00144	.00325	.00270
8.4	59.3	8.	51.3	47.2	29.2	19.	1.536	8.8	23.75	14.7	1.615	.00772	.00095	.00610	.00562	.00348	.00226	.00105	.00282	.00175
8.6	67.	8.	59.	53.25	32.75	20.5	1.595	9.2	27.5	16.5	1.666	.00780	.00093	.00686	.00620	.00381	.00239	.00107	.00320	.00192
10.8	77.	12.	63.5	54.6	34.4	20.2	1.700	9.25	29.5	16.4	1.798	.00713	.00111	.00588	.00506	.00318	.00187	.00086	.00273	.00152
17.3	147.5	16.	121.5	104.5	59.	45.5	1.287	19.5	49.	36.	1.360	.00853	.00093	.00703	.00605	.00341	.00263	.00113	.00284	.00208
9.7	76.	10.5	65.5	56.5	33.5	23.	1.455	10.	29.	18.	1.610	.00764	.00108	.00676	.00583	.00346	.00237	.00103	.00299	.00186
10.	78.	14.5	63.5	53.7	32.5	21.2	1.533	8.25	27.8	19.	1.462	.00780	.00145	.00635	.00537	.00325	.00212	.00083	.00278	.00190
9.25	85.5	8.5	77.	64.8	38.5	26.3	1.463	11.	33.2	23.5	1.412	.00925	.00092	.00834	.00700	.00416	.00284	.00113	.00359	.00254
6.6	64.	9.5	54.5	50.75	29.75	20.5	1.450	8.8	25.5	17.5	1.455	.00970	.00144	.00826	.00770	.00450	.00311	.00133	.00387	.00265
7.5	68.	7.	61.	59.	36.	23.	1.567	10.7	29.7	19.5	1.522	.00906	.00093	.00814	.00787	.00480	.00307	.00143	.00396	.00260
9.1	73.	8.5	64.5	60.5	35.	25.	1.400	10.4	30.5	21.4	1.424	.00803	.00093	.00708	.00665	.00384	.00275	.00114	.00336	.00236
13.6	103.	12.5	90.5	86.	48.	38.	1.263	15.5	39.3	30.8	1.278	.00757	.00092	.00666	.00632	.00353	.00280	.00114	.00289	.00226
11.5	88.25	11.	77.25	73.25	41.5	31.75	1.310	14.2	34.	25.6	1.330	.00767	.00096	.00672	.00636	.00361	.00276	.00123	.00296	.00223
7.25	68.	7.5	60.5	57.	33.5	23.5	1.427	8.7	28.5	20.3	1.402	.00938	.00103	.00835	.00787	.00462	.00325	.00120	.00394	.00280
6.8	62.5	6.5	56.	49.5	27.5	22.	1.250	10.2	22.5	18.2	1.236	.00920	.00096	.00825	.00728	.00404	.00324	.00150	.00331	.00268
13.6	119.	14.	115.	85.	47.	38.	1.237	18.	37.9	29.5	1.284	.00876	.00103	.00847	.00625	.00346	.00280	.00132	.00279	.00217
21.75	138.	18.	120.	101.5	58.25	43.25	1.345	18.7	48.8	36.	1.358	.00635	.00083	.00552	.00467	.00268	.00199	.00086	.00224	.00166
11.	83.	10.5	72.5	70.5	40.5	30.	1.350	13.3	32.	25.	1.280	.00755	.00095	.00660	.00640	.00368	.00273	.00121	.00291	.00227
8.2	72.5	8.	65.	61.4	36.4	25.	1.455	9.3	31.4	20.4	1.540	.00885	.00098	.00793	.00749	.00444	.00305	.00113	.00383	.00249
7.1	62.5	7.5	55.	51.8	30.	21.8	1.376	9.5	22.	16.	1.375	.00880	.00106	.00775	.00730	.00423	.00307	.00134	.00310	.00226

TABLE I—CONT'D

	WEIGHTS AND L/R RATIOS												GENERAL SEGMENTAL RATIOS								
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
						AUTHOR'S METHOD				LEWIS' METHOD											
	BODY WT. IN KG.	FRESH TOTAL HEART WT. IN GMS.	FRESH AUR. WT.	FRESH VENT. WT.	CLEAN AND FIXED VENT. WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	SEPTUM WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	RATIO TOTAL HT. WT. BD. WT.	FRESH AUR. WT. BD. WT.	FRESH VENT. WT. BD. WT.	CLEAN AND FIXED VENT. WT. BD. WT.	H. L. VENT. BD. WT.	H. R. VENT. BD. WT.	L. SEPTUM BD. WT.	L. L. VENT. BD. WT.	L. R. VENT. BD. WT.
	7.2	55.	6.5	49.	46.6	26.2	20.4	**1.285**	9.6	24.	16.6	**1.448**	.00778	.00090	.00680	.00647	.00364	.00284	.00133	.00334	.00230
	12.5	105.	10.	95.	83.7	48.3	35.4	**1.363**	16.	38.8	27.7	**1.400**	.00804	.00080	.00760	.00670	.00386	.00284	.00128	.00310	.00222
	15.5	130.	11.	119.	108.7	62.3	46.4	**1.342**	18.	53.	37.	**1.433**	.00840	.00071	.00768	.00702	.00402	.00300	.00116	.00342	.00239
	13.75	88.	9.75	78.75	71.2	42.2	29.	**1.454**	10.8	36.4	23.3	**1.560**	.00640	.00071	.00572	.00518	.00306	.00211	.00079	.00265	.00169
	10.75	97.5	9.	88.5	81.0	47.5	33.5	**1.418**	14.6	39.8	26.	**1.530**	.00906	.00084	.00824	.00754	.00442	.00312	.00136	.00370	.00242
	16.5	105.5	12.	93.5	82.8	49.	33.8	**1.450**	12.	42.4	27.5	**1.540**	.00640	.00073	.00566	.00502	.00297	.00205	.00073	.00257	.00167
	11.3	72.5	8.	64.5	59.6	35.8	23.8	**1.504**	10.8	29.6	18.4	**1.610**	.00642	.00071	.00571	.00527	.00317	.00211	.00096	.00262	.00163
	8.4	67.5	7.5	60.	55.5	31.7	23.8	**1.332**	10.3	26.	18.	**1.444**	.00805	.00089	.00715	.00660	.00377	.00284	.00123	.00310	.00214
	13.1	108.	13.	95.	80.5	43.7	37.8	**1.158**	13.1	37.6	30.	**1.250**	.00825	.00099	.00725	.00615	.00334	.00288	.00100	.00287	.00229
	12.8	109.2	15.	94.2	89.	54.	35.	**1.540**	16.5	44.5	26.4	**1.685**	.00854	.00117	.00736	.00695	.00422	.00273	.00129	.00348	.00206
	11.35	87.4	9.4	78.	68.1	39.8	29.5	**1.350**	13.0	32.5	22.8	**1.425**	.00770	.00083	.00688	.00600	.00350	.00260	.00115	.00286	.00212
	10.25	97.4	8.	89.4	82.	49.4	33.	**1.495**	14.5	40.8	26.3	**1.552**	.00950	.00078	.00870	.00800	.00481	.00322	.00141	.00398	.00257
	11.8	102.0	12.	90.	83.	46.5	36.5	**1.272**	13.5	39.5	29.5	**1.340**	.00865	.00102	.00763	.00705	.00394	.00310	.00114	.00335	.00250
	7.3	64.5	7.5	57.	57.	31.	25.8	**1.200**	10.5	25.	20.7	**1.210**	.00884	.00103	.00781	.00781	.00425	.00353	.00144	.00342	.00284
	7.55	60.4	6.5	53.2	51.5	29.3	21.5	**1.362**	10.2	24.	16.5	**1.454**	.00800	.00086	.00765	.00682	.00388	.00285	.00135	.00318	.00218
	7.1	69.5	7.5	61.2	59.5	33.	26.	**1.268**	12.	26.	20.	**1.300**	.00978	.00106	.00863	.00838	.00465	.00366	.00169	.00366	.00282
	12.15	94.	10.5	83.5	80.5	44.	36.6	**1.200**	9.3	36.	29.2	**1.234**	.00774	.00086	.00688	.00662	.00362	.00301	.00077	.00296	.00240
	15.9	120.	18.	102.	91.8	52.	38.	**1.368**	15.5	44.3	30.	**1.475**	.00754	.00113	.00642	.00577	.00327	.00239	.00098	.00279	.00189
	26.8	221.5	25.8	195.5	183.	101.	82.	**1.232**	32.	86.8	64.5	**1.344**	.00833	.00096	.00730	.00683	.00377	.00306	.00119	.00324	.00240
	9.6	74.5	7.5	67.	64.	36.5	27.	**1.352**	12.6	31.	19.8	**1.566**	.00776	.00078	.00698	.00667	.00380	.00282	.00131	.00323	.00206

TABLE I—CONT'D

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
	6.	53.5	6.0	47.5	45.5	26.5	19.2	1.380	9.2	21.8	14.2	1.536	.00893	.00100	.00792	.00758	.00442	.00320	.00153	.00364	.00237
	10.4	91.	11.	80.	77.	41.5	34.	1.220	15.3	33.2	26.5	1.252	.00875	.00106	.00768	.00740	.00399	.00327	.00147	.00320	.00254
	13.1	116.4	15.2	101.2	96.5	55.5	40.	1.388	16.	46.	32.	1.438	.00890	.00116	.00775	.00736	.00424	.00306	.00122	.00351	.00244
	15.4	134.	18.6	115.4	117.	64.5	46.	1.400	18.	55.	35.5	1.550	.00872	.00121	.00750	.00760	.00418	.00299	.00117	.00357	.00231
	17.5	173.	21.	152.	145.2	80.8	64.3	1.256	25.	68.	51.	1.333	.00990	.00120	.00868	.00830	.00462	.00367	.00143	.00388	.00292
	9.9	85.	8.	77.	74.2	40.	34.2	1.170	15.	32.5	26.5	1.228	.00858	.00081	.00778	.00750	.00405	.00346	.00152	.00328	.00268
	18.5	136.5	12.	124.5	110.	64.5	45.5	1.418	20.	53.	35.5	1.493	.00738	.00065	.00674	.00595	.00349	.00246	.00108	.00286	.00192
	20.2	118.5	13.	105.5	97.5	55.	42.5	1.294	18.5	45.2	33.8	1.336	.00587	.00065	.00523	.00483	.00272	.00210	.00092	.00224	.00167
	19.75	135.2	14.6	120.6	116.8	68.8	48.	1.432	19.5	57.2	38.5	1.486	.00685	.00074	.00612	.00590	.00348	.00243	.00099	.00290	.00195
	6.5	43.5	5.	38.5	35.5	20.2	15.3	1.320	7.	17.	11.	1.546	.00669	.00079	.00593	.00547	.00311	.00239	.00108	.00262	.00169
	6.85	68.	7.5	60.5	55.	30.	25.	1.200	11.	23.8	18.8	1.266	.00993	.00109	.00883	.00804	.00438	.00366	.00161	.00348	.00275
	13.6	110.	14.	96.	91.5	55.5	36.	1.542	16.5	47.2	27.5	1.716	.00810	.00103	.00706	.00673	.00407	.00265	.00121	.00347	.00202
	30.	180.	20.	160.	142.5	87.	55.5	1.568	25.5	72.5	44.	1.648	.00600	.00067	.00534	.00475	.00290	.00185	.00085	.00242	.00147
	12.8	111.	11.	100.	91.	53.	38.	1.395	15.5	45.	29.5	1.525	.00868	.00086	.00782	.00710	.00414	.00297	.00121	.00352	.00230
	17.5	127.3	15.	112.3	104.	64.5	39.5	1.632	21.	50.5	30.	1.683	.00728	.00086	.00643	.00595	.00368	.00226	.00120	.00288	.00171
	10.4	91.8	9.2	82.6	77.8	43.3	34.5	1.254	14.5	36.	26.5	1.358	.00882	.00088	.00794	.00748	.00416	.00332	.00139	.00346	.00255
	14.2	108.	12.	96.	92.5	57.	35.5	1.606	19.5	45.5	27.	1.685	.00760	.00085	.00676	.00650	.00401	.00250	.00137	.00320	.00190
	9.	68.	6.3	61.7	58.8	35.8	23.	1.558	12.5	27.5	18.	1.528	.00756	.00070	.00685	.00655	.00398	.00256	.00139	.00306	.00200
	6.3	46.5	6.5	40.	33.	19.5	12.5	1.560	7.	15.2	9.8	1.552	.00738	.00103	.00635	.00524	.00310	.00198	.00110	.00241	.00155
	7.9	65.	7.	58.	52.	28.	23.	1.220	11.	23.	17.	1.352	.00823	.00089	.00734	.00658	.00354	.00292	.00139	.00292	.00215
	5.8	47.	6.	41.	38.	22.	16.	1.375	8.	18.	12.	1.500	.00812	.00103	.00707	.00656	.00380	.00276	.00138	.00310	.00207
	17.5	104.	11.5	92.5	87.	55.	32.	1.720	16.	47.	25.	1.880	.00604	.00067	.00538	.00506	.00320	.00186	.00093	.00274	.00145
	2.	16.5	1.5	15.	14.5	9.	5.5	1.636	2.5	7.5	4.	1.875	.00825	.00075	.00750	.00725	.00450	.00275	.00125	.00375	.00200
	19.	170.	14.	156.	145.	81.	64.	1.265	25.	65.5	48.5	1.350	.00895	.00074	.00822	.00764	.00426	.00337	.00132	.00345	.00255
	11.65	93.3	10.	83.3	78.	46.	32.	1.438	15.	38.5	24.5	1.570	.00800	.00086	.00715	.00670	.00394	.00275	.00129	.00330	.00210
Averages	13.6	115.	12.	103.	98.	62.	36.	1.725	19.5	50.8	27.	1.880	.00847	.00088	.00758	.00720	.00456	.00265	.00143	.00374	.00183
for 80	18.75	123.5	13.5	110.	104.	60.5	43.5	1.390	20.	50.5	33.5	1.510	.00606	.00072	.00587	.00555	.00322	.00232	.00107	.00270	.00179
Males---	*12.27*	*96.78*	*11.49*	*85.38*	*77.65*	*45.00*	*32.51*	1.393	*14.05*	*37.37*	*25.86*	1.456	*.00810*	*.00096*	*.00713*	*.00651*	*.00377*	*.00273*	*.00119*	*.00312*	*.00217*

TABLE I—CONT'D

WEIGHTS AND L/R RATIOS												GENERAL SEGMENTAL RATIOS								
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
					AUTHOR'S METHOD				LEWIS' METHOD											
BODY WT. IN KG.	FRESH TOTAL HEART WT. IN GMS.	FRESH AUR. WT.	FRESH VENT. WT.	CLEAN AND FIXED VENT. WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	SEPTUM WT.	LEFT VENT. WT.	RIGHT VENT. WT.	L/R RATIO	RATIO TOTAL HT. WT. BD. WT.	FRESH AUR. WT. BD. WT.	FRESH VENT. WT. BD. WT.	CLEAN AND FIXED VENT. WT. BD. WT.	H. L. VENT. BD. WT.	H. R. VENT. BD. WT.	L. SEPTUM BD. WT.	L. L. VENT. BD. WT.	L. R. VENT. BD. WT.
15.5	107.	11.	96.	84.5	51.	33.5	1 522	15.	41.5	26.	**1.597**	.00692	.00071	.00620	.00545	.00329	.00216	.00097	.00268	.00168
10.6	78.	9.5	68.5	63.	38.	25.	1 520	12.	31.5	20.	**1.573**	.00736	.00090	.00646	.00594	.00358	.00236	.00113	.00297	.00189
20.	183.	20.	163.	135.2	80.	55.2	1.450	24.5	66.	46.5	**1.418**	.00915	.00100	.00815	.00676	.00400	.00276	.00122	.00330	.00232
18.	127.	13.	114.	100.	56.5	43.5	1 296	18.	47.5	33.5	**1.418**	.00706	.00072	.00634	.00556	.00314	.00247	.00100	.00264	.00186
9.5	75.	7.5	67.5	57.7	31.2	26.5	1.178	11.	26.5	20.2	**1.311**	.00790	.00079	.00710	.00607	.00328	.00279	.00116	.00279	.00213
9.	63.	9.	54.	46.6	27.8	18.8	1.476	8.5	24.	15.	**1.600**	.00700	.00100	.00600	.00518	.00309	.00209	.00094	.00267	.00167
7.5	59.	7.	52.	44.5	24.	20.8	1.154	6.3	20.	17.3	**1.166**	.00777	.00093	.00694	.00594	.00320	.00278	.00087	.00267	.00250
10.1	76.5	7.	69.5	60.	35.	25.	1.400	11.3	28.5	20.	**1.422**	.00760	.00069	.00688	.00594	.00346	.00248	.00112	.00282	.00198
10.7	82.5	9.2	73.4	66.5	37.5	29.	1 292	12.	32.	22.	**1.454**	.00772	.00086	.00685	.00622	.00351	.00272	.00112	.00299	.00206
9.2	88.	10.	78.	68.	39.5	28.5	1.386	12.2	32.3	22.5	**1.436**	.00957	.00109	.00849	.00739	.00428	.00310	.00133	.00351	.00245
9.35	76.5	7.	69.5	63.	36.	27.	1.334	11.7	30.8	20.	**1.540**	.00818	.00075	.00744	.00674	.00385	.00289	.00125	.00330	.00214
11.2	78.	11.	79.	69.	41.	28.4	1.440	12.5	34.5	21.8	**1.582**	.00696	.00098	.00705	.00616	.00366	.00254	.00112	.00308	.00195
7.65	53.5	5.	52.	48.5	27.	21.4	1.260	9.	21.3	16.	**1.330**	.00700	.00065	.00680	.00635	.00353	.00280	.00118	.00278	.00209
8.75	64.5	5.5	59.	57.5	36.5	21.	1.738	12.	30.	17.	**1.765**	.00737	.00063	.00675	.00658	.00417	.00240	.00137	.00343	.00194
11.4	69.	8.	61.	56.	34.	21.5	1 580	11.	28.	17.	**1.646**	.00605	.00070	.00535	.00492	.00298	.00189	.00097	.00246	.00149

TABLE I—CONT'D

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
	3.6	31.	3.5	27.5	25.	14.5	10.5	1.380	5.	12.	8.3	1.448	.00862	.00097	.00764	.00694	.00403	.00292	.00139	.00334	.00231
	4.0	33.5	4.0	29.5	25.	14.5	10.5	1.380	5.	12.	8.3	1.448	.00837	.00100	.00736	.00625	.00362	.00262	.00125	.00300	.00274
	13.3	80.	8.	72.	65.5	39.	26.5	1.470	11.5	32.5	21.	1.548	.00600	.00060	.00542	.00492	.00294	.00195	.00087	.00244	.00158
	1.8	16.	2.3	13.7	12.5	8.	4.5	1.775	2.5	6.5	3.5	1.855	.00889	.00128	.00762	.00695	.00444	.00250	.00139	.00361	.00194
	5.55	35.	4.5	30.5	28.	17.	11.	1.546	5.5	14.	8.	1.750	.00631	.00081	.00550	.00505	.00306	.00198	.00099	.00252	.00144
	18.35	122.	16.	107.	99.5	61.5	38.	1.618	18.5	50.	28.5	1.753	.00665	.00087	.00584	.00542	.00335	.00207	.00101	.00273	.00155
	18.	134.	19.	115.	96.	57.	39.	1.460	16.2	46.2	31.2	1.479	.00745	.00105	.00638	.00534	.00317	.00217	.00090	.00256	.00173
	18.	129.	16.5	113.	100.	59.5	40.5	1.470	16.5	49.	32.5	1.508	.00717	.00092	.00628	.00556	.00330	.00225	.00092	.00272	.00181
	20.15	140.	17.5	123.	111.	65.5	45.5	1.440	20.	53.	35.	1.515	.00696	.00087	.00610	.00552	.00326	.00226	.00099	.00263	.00174
	16.	140.	15.5	124.	114.	69.	45.	1.534	20.8	60.3	33.5	1.778	.00875	.00092	.00775	.00713	.00431	.00281	.00130	.00376	.00209
	7.	65.	6.	59.	55.	32.8	22.2	1.478	8.5	26.3	17.5	1.500	.00930	.00086	.00843	.00786	.00469	.00317	.00121	.00376	.00250
	8.7	67.5	6.5	60.5	51.7	28.2	23.5	1.200	10.5	23.5	18.	1.302	.00775	.00075	.00695	.00595	.00324	.00270	.00121	.00270	.00207
	11.5	108.5	11.5	97.	85.	51.	34.	1.500	14.	43.5	27.4	1.586	.00945	.00100	.00844	.00738	.00444	.00246	.00122	.00378	.00238
	7.25	72.	9.3	62.5	55.5	33.	22.5	1.468	10.2	27.	17.5	1.542	.00994	.00128	.00862	.00766	.00455	.00310	.00141	.00372	.00242
	18.25	127.	13.	114.	98.3	60.5	37.8	1.600	17.8	52.5	29.2	1.800	.00696	.00071	.00625	.00538	.00332	.00207	.00098	.00288	.00160
	12.4	77.	7.	70.	64.5	37.5	27.	1.390	11.5	32.5	21.	1.548	.00620	.00056	.00564	.00520	.00302	.00218	.00093	.00262	.00169
	17.2	103.	10.5	92.	81.	47.5	33.5	1.420	14.4	39.	26.4	1.470	.00600	.00061	.00535	.00471	.00276	.00194	.00084	.00227	.00154
	13.5	99.	13.5	85.5	74.	44.6	29.5	1.512	13.5	37.5	24.2	1.550	.00733	.00100	.00634	.00548	.00330	.00218	.00100	.00278	.00180
	16.5	161.5	18.5	142.	122.8	69.5	53.3	1.302	22.5	58.	43.	1.348	.00980	.00112	.00862	.00744	.00422	.00323	.00136	.00352	.00260
	12.5	95.5	13.5	82.5	77.	41.5	35.5	1.168	12.	35.5	27.5	1.290	.00764	.00108	.00660	.00616	.00332	.00284	.00096	.00284	.00220
Aver-	9.	76.5	9.	68.	59.	34.	25.	1.360	11.	28.8	20.2	1.425	.00850	.00100	.00756	.00656	.00378	.00278	.00122	.00320	.00225
ages	9.	87.	8.	79.	70.5	40.5	30.	1.350	11.8	32.5	26.2	1.240	.00968	.00089	.00878	.00784	.00450	.00334	.00131	.00361	.00292
for	10.4	100.	9.8	90.2	86.3	48.6	37.7	1.288	16.	41.	29.5	1.390	.00962	.00094	.00867	.00830	.00468	.00363	.00154	.00394	.00284
total	10.5	103.	8.	9.5	91.5	56.	35.5	1.578	16.3	43.5	26.	1.673	.00982	.00076	.00905	.00872	.00534	.00338	.00155	.00414	.00248
200	11.5	95.	12.5	82.5	82.	45.	37.	1.216	13.8	38.	30.2	1.224	.00825	.00109	.00717	.00713	.00391	.00322	.00120	.00330	.00263
normal																					
dogs ---	*11.37*	*89.38*	*10.73*	*78.64*	*71.03*	*41.25*	*29.74*	1.398	*12.98*	*34.26*	*23.66*	1.461	*.00798*	*.00097*	*.00789*	*.00635*	*.00369*	*.00265*	*.00116*	*.00300*	*.00212*

series of twenty normal dogs' hearts, divided by Müller's method records the only figures thus far reported that are at all adequate. In this series the use of the obsolete method of Müller for separating the ventricles probably accounts for the far too great a variation in the L/R (left ventricular to right ventricular) weight ratios which I have calculated. In Stewart's series the H.W./B.W. ratio ranges from 0.00609 to 0.00856, the average being 0.00721. I have found the left ventricular weight right ventricular weight (L/R) ratio for Stewart's series to range from 1.460 to 2.590 with an average of 1.950. The left ventricular weight body weight (L.V.W./B.W.) ratio varies from 0.00226 to 0.00358 with an average of 0.00315. The right ventricular weight body weight (R.V.W./B.W.) ratio varies from 0.00122 to 0.00215 with an average of 0.00158. The septum weight body weight (S.W./B.W.) ratio varies from 0.00114 to 0.00215 with an average of 0.00166. The total cleaned and fixed ventricular weight body weight (C.&F.V.W./B.W.) ratio varies from 0.00515 to 0.00760 with an average of 0.00647. The auricular weight body weight (A.W./B.W.) ratio varies from 0.00058 to 0.00111 with an average of 0.0080.

NEW CONTROL DATA

With this small series, divided by a more or less obsolete method (Müller's), as the only standard normal control values, it was considered essential first to establish a broad standard. To this end the hearts of two hundred normal dogs of various sizes, types and mongrel breeds have been divided by the author's method and by Lewis' method.

In Table I the various weights, body total and sectional, together with the various ratios, have been recorded. The columns in order contain:

(1) Body weight of the dogs in kilograms;
(2) Total fresh heart weight in grams;
(3) Fresh auricular weight in grams;
(4) Fresh ventricular weight in grams;
(5) Cleaned and fixed ventricular weight in grams;
(6) Left ventricular weight in grams after separation by author's method;
(7) Right ventricular weight in grams after separation by author's method;
(8) Ratio of left ventricular weight to right ventricular weight after separation by author's method. (Bold type.)
(9) Septal weight after separation by Lewis' method.
(10) Left ventricular weight after separation by Lewis' method;
(11) Right ventricular weight after separation by Lewis' method;
(12) Ratio of left ventricular weight to right ventricular weight after separation by Lewis' method. (Bold type.)
(13) Ratio of the total fresh heart weight to the body weight;
(14) Ratio of the fresh auricular weight to the body weight;
(15) Ratio of the fresh ventricular weight to the body weight;
(16) Ratio of the cleaned and fixed ventricular weight to the body weight, which is the same as the cleaned fresh, since the weight after fixation is brought back to the fresh weight;
(17) Ratio of the left ventricular weight, after separation by the author's method, to the body weight;

(18) Ratio of the right ventricular weight, after separation by the author's method, to the body weight;
(19) Ratio of the septal weight after separation by Lewis' method to the body weight;
(20) Ratio of the left ventricular weight after separation by Lewis' method to the body weight;
(21) Ratio of the right ventricular weight after separation by Lewis' method to the body weight.

The various figures for the hearts of eighty normal female dogs and eighty normal male dogs, for twenty dogs that died at operation, and for twenty dogs that were operated upon, but showed no valve lesions, have been set down in order, with the mean arithmetical averages for each column and for the whole series of 200 dogs in italics at the end of each group.

TABLE II

IMPORTANT AVERAGES FOR VARIOUS GROUPS, MAXIMUM, MINIMUM VALUES AND GRAND TOTAL AVERAGES

	L/R(H)	L/R(L)	H.W./B.W.	C.&F.V.W./B.W.	L.V.(H)/B.W.	R.V.(H)/B.W.	L.V.(L)/B.W.	R.V.(L)/B.W.
80F.	1.390	1.441	.00792	.00623	.00361	.00262	.00299	.00210
80 M.	1.393	1.456	.00810	.00651	.00377	.00273	.00312	.00217
20 OP.	1.428	1.520	.00759	.00606	.00305	.00251	.00295	.00201
20 Sc.	1.418	1.496	.00816	.00653	.00382	.00269	.00317	.00214
Max.	1.773	1.880	.00994	.00872	.00472	.00400	.00388	.00284
Min.	1.153	1.150	.00600	.00467	.00268	.00178	.00222	.00154
Ave. 200	1.393	1.461	.00798	.00635	.00369	.00265	.00306	.00212

TABLE III

STATISTICAL TABLE FUNCTIONS

	L/R(H)	L/R(L)	HW/BW	C&FVW/BW
Mean	1.398	1.459	.00798	.00636
Median	1.390	1.454	.00796	.00672
Mode Pearson's III	1.388	1.450	.00765	.00675
Standard Deviation	0.2705	0.3168	.0001036	.0007521
Skewness ratio	.413	.353	.60636	.40412

TABLE IV

CORRELATION COEFFICIENTS

L/R(H)	Σxy	0.95885562
L/R(L)	Σxy	0.95055205
H.W./B.W.	Σxy	0.91520807
C.&F.V.W./B.W	Σxy	0.90582930
L.V./ $\overset{(H)}{B.W.}$	Σxy	0.86775584
L.V./ $\overset{(L)}{B.W}$	Σxy	0.91045902
L/R(H)/B.W.	Σxy	.0076985632
L/R(L)/B.W.	Σxy	.029285724
L/R(H)/C.&F.V.W.	Σxy	.0074650309
L/R(L)/C.&F.V.W.	Σxy	.048952101

In Table II the important averages of each group and for the whole series of two hundred normal dogs are given. In general the figures

are remarkably uniform and constant. The averages for male dogs uniformly show slightly higher values than do those for the females. The average L/R ratios are greater in the smaller series than in the larger series.

The mean arithmetical averages, with the minimum and maximum figures of the more important ratios for the control series from the two hundred normal dogs, will bear special mention. The $L/R^{(H)}$ (left ventricular to the right ventricular weight separated by the author's method) is 1.393 with a minimum of 1.153 and a maximum of 1.773. The $L/R^{(L)}$ (left ventricular to the right ventricular weight separated by Lewis' method) is 1.461 with a minimum of 1.150 and a maximum of 1.880. The H.W./B.W. (fresh total heart weight to the body weight, is .00798 with a minimum of .00600 and a maximum .00994. The C. and F.V.W./B.W. (the cleaned and fixed ventricular weight to the body weight) is .00635 with a minimum of .00467 and a maximum of .00872. The $L.V.W./B.W.^{(H)}$ (the left ventricular weight by the author's method to the body weight) is .00369 with a minimum of .00268 and a maximum of .00472. The $R.V.W.^{(H)}/B.W.$ (the right ventricular weight by the author's method to the body weight) is .00265 with a minimum of .00178 and a maximum of .00400. The $L.V.W./B.W^{(L)}$ (the left ventricular weight by Lewis' method to the body weight) is .00306, with a minimum of .00222 and a maximum of .00388. The $R.V.W./B.W.^{(L)}$ (the right ventricular weight by Lewis' method to the body weight) is .00212 with a minimum of .00154 and a maximum of .00284.

STATISTICAL STUDIES OF THE CONTROL DATA

The author is deeply indebted to Professor H. C. Carver and the Department of Mathematical Statistics of the University of Michigan for the statistical studies, detailed in Tables III and IV, of the data obtained from the two hundred normal control dogs.

The important statistical functions[10] are as follows: For the $L/R^{(H)}$ ratio, the mean is 1.398, the median 1.390, the mode (Pearson's III) 1.388. The standard deviation 0.2705 and the skewness 0.413. For the $L/R^{(L)}$ ratio, the mean is 1.459, the median 1.454, the mode (Pearson's III) 1.450, the standard deviation 0.3168 and the skewness 0.353. For the H.W./B.W. ratio, the mean is .00798, the median .00796, the mode (Pearson's III) .00765, the standard deviation .0001036 and the skewness .60636. For the C. and F.V.W./B.W., the mean is .00635, the median .00672, the mode (Pearson's III) .00675, the standard deviation .00075214 and the skewness .40412.

The correlation coefficients (Σxy) obtained showed that practically *no* correlation exists between the $L/R^{(H)}$ and the body weight ($\Sigma xy = .0076856$); between the $L/R^{(L)}$ and the body weight ($\Sigma xy = .0292857$); between the $L/R^{(H)}$ and the cleaned and fixed ventricular

weight (Σxy .0074650); between the $L/R^{(L)}$ and the cleaned and fixed ventricular weight (Σxy = .048952). There is, however, very *good* correlation between the left and right ventricular weights by the author's method (Σxy = 0.95885); between the left and right ventricular weights by Lewis' method (Σxy = 0.95055); between the total fresh heart weight and the body weight (Σxy = 0.915208); between the cleaned and fixed ventricular weight and the body weight (Σxy = 0.005829); between the left ventricular weight by the author's method and the body weight (Σxy = 0.86775); between the left ventricular weight by Lewis' method and the body weight (Σxy = 0.910459).

SUMMARY

The standard methods for the preparation of hearts and the separation of ventricles are given in detail.

The complete data on two hundred normal dogs' hearts are recorded as a standard control series. The separation of the ventricles was accomplished both by the author's method and Lewis' method. The statistical studies of the data may be interpreted as favoring the author's method, but the differences are relatively slight. Furthermore, the author offers his method mainly as a step to facilitate a more accurate separation of the ventricles by Lewis' method and to serve as a check of the accuracy of the weighings.

In conclusion, it might be stated that this preliminary report may serve to standardize the methods and supply an adequate normal control series for dogs' hearts.

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OBSERVATION ON THE PROGRESSION OF CHRONIC VALVULAR HEART DISEASE*

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THE progressive nature of chronic valvular heart disease, while recognized, has apparently not been sufficiently appreciated. There have been very few instances, to my knowledge, in which this feature has been carefully studied in a series of cases. Mackenzie[1] very early saw the importance of this type of investigation and thus greatly extended our knowledge of the course of chronic valvular heart disease. Poynton[2] has made interesting and valuable observations on the progress of cardiac disease in children with rheumatic fever. More recently Coombs[3] has written a book on rheumatic heart disease, based on observations covering a period of years.

In the present investigation the progression of the cardiac disability in forty patients with chronic valvular heart disease was carefully followed for a period varying from three to six years. These patients were seen at frequent intervals and questioned in regard to symptoms, and the changes in the physical findings were noted. Frequently the size of the heart was checked by the x-ray and in many instances routine electrocardiograms were taken.

These forty patients are divided for convenience into four groups, according to the type of valve lesion present at the time of the first examination: (1) mitral stenosis; (2) mitral stenosis and regurgitation; (3) mitral regurgitation and (4) mitral and aortic regurgitation.

In seven the initial diagnosis was mitral stenosis. The ages of the group varied from eighteen to thirty-five years. In four the age was under twenty-five years. Three gave a history of having had rheumatic fever between the ages of seven and ten years which was probably responsible for the initial cardiac infection. In the remaining four, no definite etiological factor was found in the past history. In the rheumatic group the duration of the cardiac lesion was estimated to be eleven, thirteen and fifteen years respectively. Two of the remaining four had had, to their knowledge, some trouble with the heart for four to five years. In the other two the cardiac lesion was first discovered a few months prior to their coming under observation.

In each of the seven patients there was a moderately high-grade mitral stenosis when first examined. Three were followed for five,

*These observations were made in the Cardiac Clinic of the Central Free Dispensary, Rush Medical College, Chicago.

two for four, and the remaining two for three years. During the period of observation three died from cardiac failure. In one the onset of a permanent auricular fibrillation hastened the termination. In two the cardiac rate was persistently rapid and each was frequently observed to have a temperature of from 99.2 to 100° F. which was never explained other than on a cardiac basis. In each case routine electrocardiograms were taken and on different occasions these showed a delay in the conduction over the auriculoventricular bundle. Each of these patients was thought to have an active cardiac infection. Blood cultures were negative and embolic manifestations were absent. Finally the signs of cardiac failure appeared, which were followed in a few months by death.

In another patient permanent auricular fibrillation became established two years ago. In the beginning the absolute irregularity appeared in paroxysms lasting from a few minutes to hours. Finally, after the irregularity apparently became established, the normal mechanism was readily restored by quinidine sulphate. The mechanism would revert again to the auricular fibrillation within a few hours or days. This patient was followed for five years and during this period the cardiac disability, judging from the response to exertion, definitely progressed. The progression of the cardiac disability was far more apparent after the onset of the auricular fibrillation.

In another patient who has been followed closely for four years a cardiac irregularity, in the form of premature auricular contractions, was first noted six months ago. Two months later he returned to the clinic because of palpitation of the heart and shortness of breath. He was found to have a paroxysmal auricular fibrillation which lasted for thirty-six hours. He has since had further attacks. The auricular fibrillation will no doubt soon become permanently established. Even though there has been no other change in the auscultatory findings and no demonstrable increase in the size of the heart during the period of observation, the appearance of the auricular fibrillation indicates a progression of the cardiac disability.

In the two remaining patients still living, there has apparently been no change in the cardiac condition during three and four years respectively. They have sedentary occupations and appreciate the importance of protecting themselves against infections and avoiding overexertion. One of these men had a permanently established auricular fibrillation when first seen. According to his story this had probably been present for at least five years, yet there had never been any symptoms of cardiac failure, and on the numerous occasions when he was examined, the cardiac rate was never above 85 to the minute.

In ten patients the diagnosis, at the time of the first examination, was mitral stenosis and regurgitation. In eight the ages were under

fifteen years. The ages of the remaining two were seventeen and thirty-five years, respectively. Five of the ten gave a history of rheumatic fever between the ages of six and ten years. In four there had been repeated attacks. Three of these had frequent slight joint manifestations during the period of observation. Three of the remaining ten stated that they had had repeated attacks of sore throat. One had had, in addition, chorea. There were thus only two in whom it was not possible to find a probable etiological basis for the cardiac disease in the past history.

Three of these patients were followed for five years, five for four years and two for three years. Seven died from cardiac failure. In three the course was in many respects very similar and may be fairly typically illustrated by the following case:

J. D., aged seventeen years, was first examined in May, 1917. She gave a history of having had chorea at twelve years and had had, at times, slight rheumatic joint manifestations. There were no cardiac symptoms. The apex impulse was just outside the midclavicular line. A systolic apical murmur was heard and there was a presystolic roughening which was regarded as indicating a beginning mitral stenosis. During October, 1919, she complained for the first time of precordial pain; and stated that she became short of breath rather easily. The apex impulse was now more diffuse and was well outside the midclavicular line. A definite presystolic murmur and a palpable thrill were recorded. The cardiac rate was rapid and there was thought to be an active cardiac infection. She had, during the winter of 1920, several attacks of tonsillitis, one of which was followed by erythema nodosum. She again complained of shortness of breath and was sent to the hospital where she was confined to bed for several weeks. Four months later the tonsils were removed. Within a few weeks after the operation she again experienced precordial distress and shortness of breath. The area of cardiac dullness was observed to be increased greatly over that recorded in 1919. There was some improvement with another prolonged stay in the hospital. Later the cardiac disability rapidly progressed and she died in May, 1921.

The course of the cardiac disease in the other two patients was similar, in that the disability rapidly progressed and terminated fatally within four and six years, respectively. The presystolic murmurs became more harsh and extended further back into the diastolic period. The thrills became more evident and the size of the heart gradually increased. In these two instances there were likewise frequent recurring infections which were considered to be important factors in the progression of the cardiac disease.

In two patients the signs and symptoms of a chronic adhesive pericarditis developed. Each gave a history of repeated attacks of tonsillitis and rheumatic fever. In both the cardiac damage was extensive when first seen. There was, however, no evidence of portal obstruction and adhesions of the pericardium could not be demonstrated. Later the x-ray findings were suggestive of pericardial adhesions. A Broadbent's sign was discovered and fluid appeared in the abdomen. There-

after until death, one and one and a half years later respectively, it was frequently necessary to remove the fluid from the peritoneal cavity by abdominal paracentesis.

The remaining patient of those who died is of particular interest because of the development of an aortic regurgitation and the response to a tonsillectomy. He was first examined in 1919. Nine months later a questionable diastolic aortic murmur was heard. Within a few months the origin of the murmur was evident. The boy was advised to have his tonsils removed when his condition would permit. He, however, did not report again until three years later. His heart had greatly increased in size and the signs of aortic regurgitation were more evident. There was a history of recent attacks of tonsillitis. The cardiac rate was rapid and a temperature of 99.4° F. was recorded. The boy was hospitalized for a time and later the tonsils were removed. Very shortly following the operation the signs and symptoms of cardiac failure appeared and the patient died. It was felt that the operation probably had been done too soon following the acute tonsillar infection and had precipitated the cardiac failure.

In two of the three patients of this group still living, the cardiac disability definitely progressed; one was on the verge of cardiac failure when last seen. The other child was in poor general condition and complained of recurring attacks of pains in the legs that were undoubtedly rheumatic in origin.

There were eighteen patients with the findings of a mitral regurgitation when first examined. Fourteen of these were children. The youngest was one and one-half years old when first seen. In the remaining thirteen the ages varied from seven to thirteen years. Nine of the fourteen either gave a history of having had attacks of rheumatism or had rheumatic joint manifestations during the period of observation. Five of these had had, in addition, frequent attacks of tonsillitis and two chorea. In one there was a history of chorea alone. Two of the remaining children had had, according to their mother, frequent attacks of sore throat. Thus there were only two in whom a probable etiological factor was not found in the past history. In one of the adults the acute endocarditis was discovered shortly following an attack of rheumatic fever.

This group was by far the most interesting from the standpoint of the progression of the valvular defect. Seven were seen during, or a short time following, the onset of the cardiac infection. In ten there was a very evident progression of the cardiac disease as indicated by the increase in the size of the heart and the appearance of new murmurs. Two died during the period of observation.

R. C., the youngest of the group, was first examined when one and one-half years old following an attack of tonsillitis and painful joints. The heart was very irritable, slightly increased in size and a systolic apical murmur was heard. The

child was pale and had a slight daily rise of temperature. Even though she was hospitalized for six months and the tonsils removed, the cardiac disease rapidly progressed and she died within about three years following the onset of the infection. The heart gradually increased in size and the murmur became more harsh in character.

The other patient in whom the cardiac disease terminated fatally was followed for six years. He was first examined at the onset of the cardiac infection during an attack of rheumatism. At the necropsy the heart weighed, approximately, 600 grams and the auriculoventricular opening would barely permit the introduction of a lead pencil. The first evidence of the mitral stenosis was recorded about three years after the onset of the infection. Two years later auricular fibrillation became permanently established. Finally, three months prior to death, a complete heart-block developed.

In five an aortic regurgitation developed. Three of these were adults and two children. The children were seen at more frequent intervals and the date of the appearance of the new murmurs was more accurately known.

F. P. aged eight years, was first examined in May, 1921. The apex impulse was just outside the midclavicular line in the fifth interspace. A soft blowing systolic murmur was heard at the apex. Three months later, following a period of fever, a very faint diastolic murmur was detected over the aortic area and to the left of the sternum. Within a few months the murmur could be heard very easily.

G. W. aged eleven years, first visited the clinic in July, 1921. She gave a history of frequent attacks of sore throat and at times had complained of vague pains in the legs. There was some question at the time as to whether there was a definite organic valvular disease. She was last examined in August, 1924. The left border of the cardiac dullness in the fifth interspace was approximately in the midaxillary line. There was a definite presystolic murmur at the apex and a faint diastolic murmur, which was thought to be aortic in origin, was heard over the second and third left interspaces. During this period the child was hospitalized on three different occasions for periods of absolute rest and the tonsils were removed.

In the remaining three patients, in whom it was felt that the cardiac disease progressed, conduction defects were discovered during periods of fever. In one a delayed conduction time of the auriculoventricular bundle persisted for more than a year. During a part of this time there was a complete auriculoventricular dissociation which disappeared following the administration of atropine. A similar derangement in the cardiac mechanism has since been observed in an adult following acute tonsillitis, which also was eliminated by atropine.

There were five patients with aortic and mitral regurgitation. Their ages ranged from seven to nineteen years. Three gave a rheumatic history. In one the cardiac disease terminated fatally. In two of the remaining the cardiac disease progressed. In one there was an active cardiac infection during the earlier months of observation indicated by fever, rapid heart action and a conduction defect as shown by the electrocardiogram. Later the infection seemed to subside and the patient was in satisfactory condition when last seen. One of the

two in whom there has been no evidence of progression of the cardiac disease has gone through two pregnancies without any demonstrable change in the size of the heart and the character of the murmurs.

DISCUSSION

In the forty patients with chronic valvular heart disease, followed for a period varying from three to six years, the cardiac disability progressed in twenty-eight (70 per cent). Thirteen died from cardiac failure during the period of observation. In three the physical findings were those of mitral stenosis. In one of these an auricular fibrillation became established before the symptoms of cardiac failure appeared. In the other two, active cardiac infections were regarded as being responsible for the rapid progression of the cardiac disease.

Six of the ten patients diagnosed as having mitral regurgitation and stenosis when first examined eventually died. In three the course was similar in that it was progressive and influenced by recurring infections. The heart gradually increased in size and the presystolic murmurs became more harsh and occupied more of the diastolic period. In one instance the murmur, when first heard, was no more than a presystolic roughening. In two of the six the clinical picture of chronic adhesive pericarditis developed. In the remaining one an aortic regurgitation appeared.

Two patients were followed during the entire course of the cardiac disease. In one the initial infection occurred at the age of one and one-half years following an acute sore throat and an attack of rheumatism. The disease rapidly progressed and the child died within three years. In the other a very high grade mitral stenosis, which was demonstrated at necropsy, developed in six years.

The cardiac disease definitely progressed in fifteen of the twenty-seven still living. In all instances the heart increased in size. In three aortic regurgitation, and in one a mitral stenosis, developed. Five had, at some time, conduction defects of the auriculoventricular bundle. In one an auricular fibrillation became established and another had paroxysms of absolute irregularity.

It is appreciated that the number of patients in this series is too small from which to draw conclusions in regard to the incidence of the progression of the cardiac disability in those with chronic valvular heart disease. Furthermore, these studies were made on dispensary patients. In the majority the living conditions were poor. The children, because of economic stress, were neglected in many instances. The adults often were obliged to do work of a type for which they were not physically fit. These factors, which undoubtedly favored the progression of the cardiac disease in this group of patients, might, in a large measure, be disregarded in those with better educational qualifications and under improved economic circumstances.

These studies, however, emphasize the progressive nature of chronic valvular heart disease. It is felt that this feature has not been sufficiently recognized in the treatment of this condition. The physician is too prone to disregard the valvular defect when the functional capacity of the heart seems satisfactory and not to adopt measures to safeguard the individual against the progression of cardiac disease. A comprehensive diagnosis should include, first, the etiological factor, and whether or not this is still present; second, the progress and the extent of the cardiac damage, and lastly the presence or absence of an active infection.

There are several factors which may influence the course of chronic valvular heart disease. In this study, however, the persistence of the initial infection or the frequent recurrence of an active cardiac infection was considered to be largely responsible for the rapid progression of the disease in most instances.

It is often very difficult to determine whether or not there is an active cardiac infection. The presence of a daily elevation of temperature and a persistent acceleration of the cardiac rate may be the only clinical manifestations. The fever may be slight and perhaps may not exceed 99.2° F. or 99.8° F. in the afternoon. The increase in the cardiac rate is out of proportion to the temperature readings. In the vast majority, with these findings, in the absence of other demonstrable causes, the diagnosis of an active cardiac infection may be verified later by the appearance of other manifestations. The presence of precordial pain is suggestive of the possibility of an active cardiac infection. The majority of the patients in our series in whom the disease was definitely progressing complained at some time of pain in the precordium. This pain was intermittent in type and was apt to be sharp and "sticking" in character. It usually would disappear in a few days. In practically all instances, the patient was regarded as having an active cardiac infection and later developments proved this to be true. The distress was thought to be due to a possible slight pericardial involvement. In four instances a transient pericardial rub was discovered, and in three others conduction defects were found by means of the electrocardiogram. Coombs[3] has mentioned the frequency with which the pericardium becomes involved in rheumatic heart disease and cites the postmortem records of the Bristol General Hospital. These records showed that 100 per cent of those who died in the first decade with rheumatic heart disease had pericardial lesions; 83 per cent in the second; 41 per cent in the third; 23 per cent in the fourth, and after the age of forty, 26 per cent.

In doubtful cases the electrocardiogram may give the additional information necessary to make a positive diagnosis. Routine curves taken at weekly intervals not infrequently will show conduction defects at some time if there be an active cardiac infection. The con-

duction defect is usually in the form of a slight prolongation of the P-R interval which frequently disappears within a few days. The incidence of this type of heart-block in cardiac infections is difficult to estimate. Parkinson, Gunson and Gosse[4] observed this condition in 30 per cent of those with an active rheumatic carditis. Coombs,[3] on the other hand, states that he has encountered only six instances in which there was an interference with the conduction over the auriculo-ventricular bundle. In our series in which a particular effort was made to discover possible conduction defects, the incidence was much higher than that reported by Coombs and approached that cited by Parkinson and his co-workers. The frequency with which a prolongation of the P-R interval may be detected no doubt will depend somewhat on the care with which it is sought.

Cohn and Swift[5] recently have recorded changes in the T-wave of the electrocardiogram during the course of acute rheumatic fever. This feature has been observed in the present study. It is possible that this alteration in the T-deflection may be of value in determining the presence of an active infection.

SUMMARY

1. In forty patients with chronic valvular heart disease the progress of the cardiac disability was studied for a period of three to six years. The disease definitely progressed in twenty-eight, or 70 per cent. In thirteen of the twenty-eight the condition terminated fatally.

2. The progression of the disease was indicated by an increase in the size of the heart. In some there was, in addition to this feature, a change in the character of the murmur or the development of a new murmur. In others auricular fibrillation became established or conduction defects were found by means of the electrocardiogram.

3. An active cardiac infection was considered to be largely responsible for the progression of the disease.

4. The presence of an active infection is often difficult to determine in a heart that is already damaged. A rapid cardiac rate and a slight daily elevation of temperature may be the only clinical manifestations. Pain in the precordium is a very suggestive symptom. In doubtful cases the electrocardiogram may give sufficient information to establish the diagnosis.

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BASAL METABOLISM IN ORGANIC HEART DISEASE*

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DURING the past year and a half we have been interested in the basal metabolism in patients with organic heart disease with decompensation.[1] Seventeen cases observed carefully, with double that number with less complete data, showed substantially the same results. Seventy-five per cent of these cases entering the hospital with various degrees of decompensation showed a definite and constant increase in their basal metabolic rate; 25 per cent showed a normal rate or one below normal. Of those showing an increase, the highest reading obtained was 66 per cent above normal, the lowest 11.8 per cent above, the average being 39 per cent above normal. As compensation returns, the basal metabolic rate drops to normal or below; in cases where compensation does not return the basal metabolic rate remains high. In one case of rheumatic heart disease with both aortic and mitral involvement, with ultimate death from heart failure, the average of the entrance readings was 15 per cent above normal; later the rate rose to 22 per cent above and remained at 20 per cent just before exitus.

The basal metabolic rate was not related to the type of cardiac valve or muscle involvement, nor to edema, cyanosis, arrhythmia, or electrocardiographic findings, but only to the degree of heart muscle failure and the pulse and respiratory rates.

Since our preliminary report,[1] we have occupied ourselves with attempts to secure data on the factor or factors responsible for this increase in basal metabolism during cardiac decompensation, and the present paper consists in a report of this data.

Before turning to a consideration of this material we wish to mention briefly a number of papers which have appeared in the literature since the publication of our preliminary report and which have a direct bearing on this phase of the problem. Boothby and Willius[2] in an extensive report on 217 cases of organic heart disease state that "in the routine determinations of the basal metabolic rate in patients with cardiac disease, the level of the metabolism is found to be slightly elevated above the DuBois standard more frequently than in strictly normal subjects. This elevation is independent of electrocardiographic findings and of the type, character and degree

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of the organic heart lesion." They conclude that the two most probable factors for this increase in basal metabolism are "the actual increase in muscular work required in labored respirations and the subjective sensation of distress with resultant nervousness and fear from the application of the mask or mouthpiece."

In connection with the last named factor, a report by Ziegler and Levine[3] on the influence of emotional reactions on basal metabolism is interesting and important. They showed that certain psychoneurotic individuals, without goiter but with various worries, unpleasant memories or thoughts of emotion-producing aspects of their past history, respond by an increased metabolic rate. As Boothby and

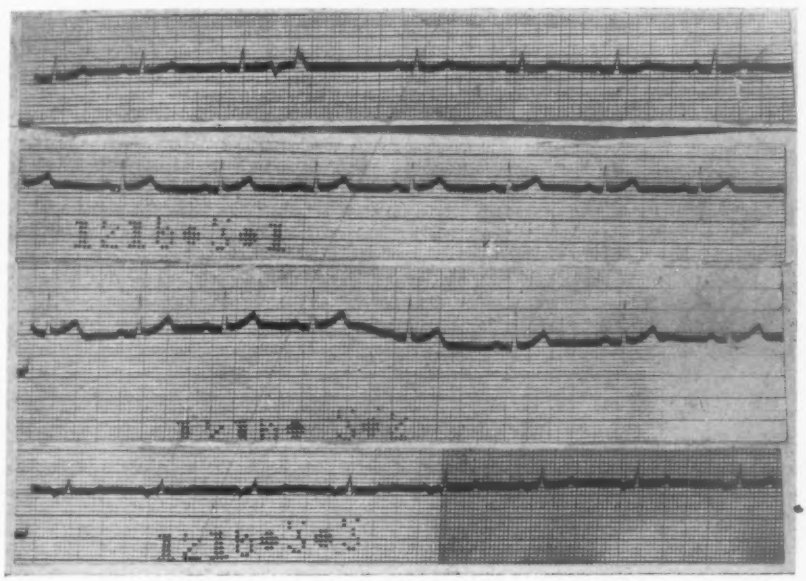

Fig. 1.—Patient A. F. S. Case of paroxysmal auricular tachycardia taken simultaneously with B. M. R. before attack. First lead shows solitary auricular extrasystole with ventricular aberration. Sinus rhythm rate 67. B. M. R. 6 per cent below normal.

Willius point out, this factor of emotional reaction is of particular importance in the evaluation of increased basal metabolism in cardiac disease, because of the anxiety and apprehension which many of these patients possess. However, in this series, it is suggestive that in the group of cardiac neuroses, where *a priori* one would expect these factors to be particularly prominent, only three cases showed a constantly high rate. DuBois,[4] discussing the probable factors concerned, concludes "that there is nothing in heart disease of itself that alters the metabolism, but that the increased activity of the muscles of respiration causes an increased oxygen consumption. It is also possible that the increased work of the heart helps to raise the metabolism to a slight extent."

In the present paper we wish to report; (1) the changes in basal metabolism in a case of paroxysmal auricular tachycardia before and during a paroxysm of tachycardia, and (2) the changes in basal metabolism, the result of artificially increased respiratory rate.

CHANGES IN BASAL METABOLISM IN A CASE OF PAROXYSMAL AURICULAR TACHYCARDIA BEFORE AND DURING THE PERIOD OF TACHYCARDIA

Barcroft, Bock and Roughton[5] report the case of a university student of twenty-two years, with repeated attacks of tachycardia, who

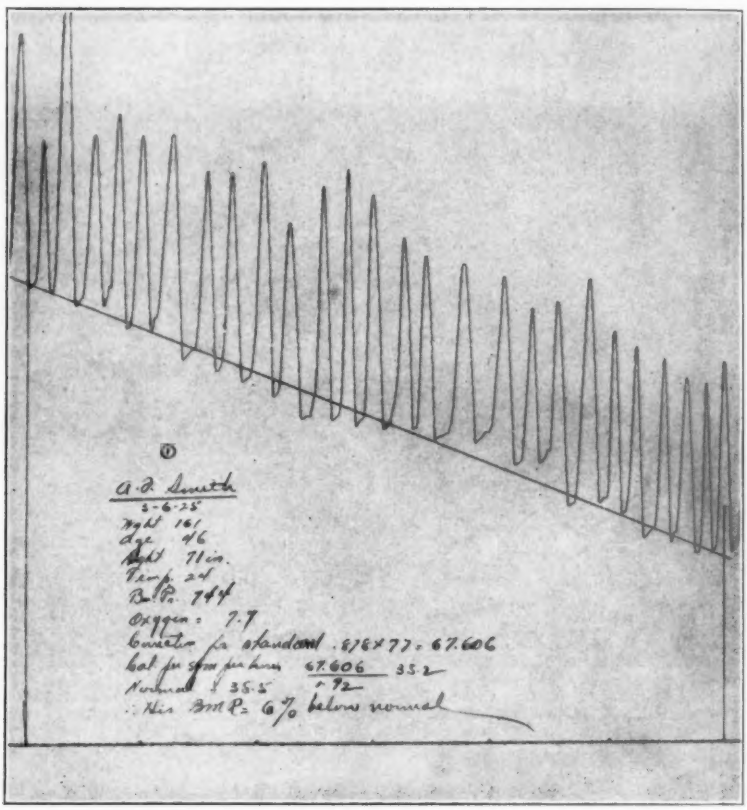

Fig. 2.—Respiratory tracing of patient A. F. S., with paroxysmal auricular tachycardia during period of normal sinus rhythm (control). B. M. R. 6 per cent below normal. Respiratory rate 4.3 per minute. Cardiac rate 67 per minute.

showed a considerable lowering of the total oxygen consumption during two attacks of tachycardia. In a previous attack, however, the oxygen consumption had been normal and they conclude that the lowering may not take place throughout the whole attack.

Dieuaide's[6] case of paroxysmal tachycardia on the other hand showed an increase of 16.7 per cent above normal, which he attributed to the added work of the heart and lungs rather than to some more fundamental change.

The clinical history of the patient we wish to report is as follows: Mr. A. F. S., a telephone adjuster, aged forty-four years, has suffered with attacks of sudden rapid beating of the heart since his boyhood, starting originally while playing football. During the past two years he has had almost daily attacks. He can usually start them at will by exercise, by turning and lying on his right side, etc. Likewise he can terminate an attack by deep breathing, bending at the waist, raising his leg, stretching, standing erect against a wall, squatting, etc. The attacks have been more frequent since an attack of encephalitis in February, 1919. Systolic blood pressure is 120 mm., diastolic 65. Wassermann reaction is negative. Fluoroscopy reveals

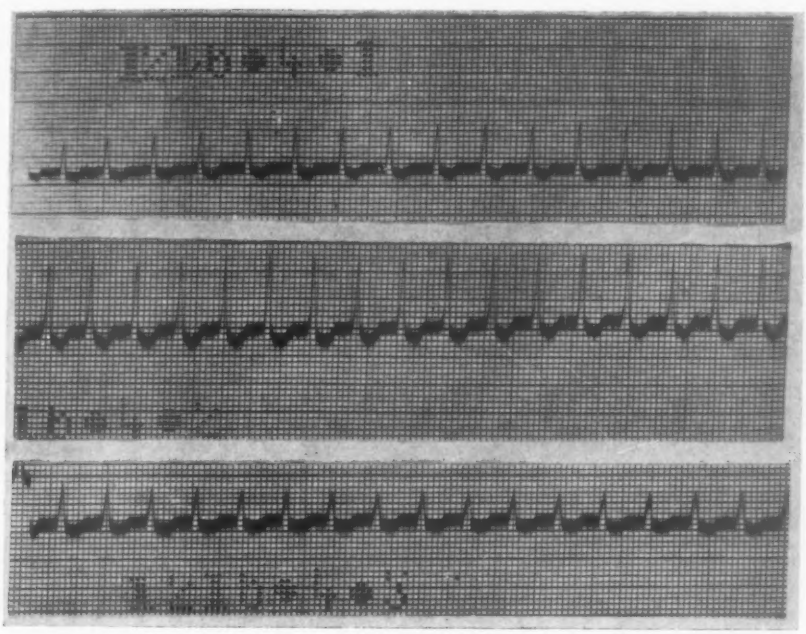

Fig. 3.—Patient A. F. S. during an attack of paroxysmal tachycardia. Curve taken simultaneously with B. M. R. Ventricular rate 187. B. M. R. 5.1 per cent above normal.

a slight widening of the ascending aortic arch just above the base of the heart, amounting almost to a diffuse aneurysm at this point. During a paroxysm the heart appears somewhat smaller in the transverse diameter than between attacks (sinus rhythm). The attacks are quite well controlled by small amounts of quinidine with occasional periods of small doses of digitalis.

As this patient could bring on an attack of tachycardia almost at will, we considered him a favorable case for making the experiment. On the morning of the test, after the usual overnight fast, he came to the heart station, where he rested in the prone position for the

usual 30 minutes. At the end of this time a control electrocardiogram was taken, which showed in Lead II a normal sinus rhythm with a solitary extrasystole, probably of auricular origin. The basal metabolic rate was then estimated with a portable Benedict-Roth machine, a second electrocardiogram being taken simultaneously, showing a sinus rhythm with a rate of 67 (Fig. 1). His control metabolism showed his basal metabolic rate to be 6 per cent below normal, a

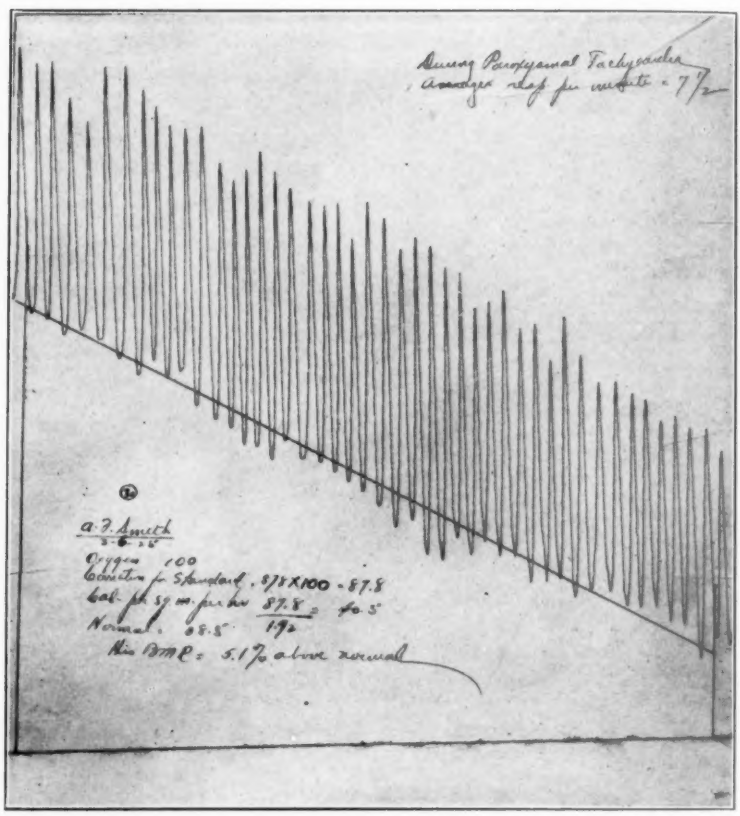
Normal Paroxysmal Tachycardia
Average rate per minute = 7½
a. F. Smith
Oxygen 100
Correction for Standard 87.8 X 100 = 87.8
Cal. per sq m per hr 87.8 = +6.5
Normal 81.3
B.M.R. = 5.1% above normal

Fig. 4.—Patient A. F. S. respiratory tracing during period of rapid heart action (paroxysmal tachycardia). B. M. R. 5.1. per cent above normal. Respiratory rate, 7.5 per minute. Cardiac rate 187 per minute.

graph of his respirations being slow (Fig. 2), his respiratory rate being exceptionally slow—an average of 4⅓ per minute.

The patient then induced a paroxysm of tachycardia by turning and lying on his right side, simultaneous metabolism and electrocardiographic readings again being taken. Fig. 3 gives the electrocardiogram taken during the period of tachycardia, showing a rate of 187—approximately 2.5 times the control. Fig. 4 shows his respiratory tracing at this time, with a basal metabolic rate of 5.1 per cent above

normal—a total rise of 11.1 per cent over the control and a respiratory rate of 7½ times per minute—a little less than double that before the attack. In other words, his increased metabolic rate was accompanied by an increase in both the cardiac and respiratory rate, a result which fits in with the belief expressed by DuBois in reference to increased metabolic rate during decompensation, namely, that the increased activity of the muscles of respiration as well as the in-

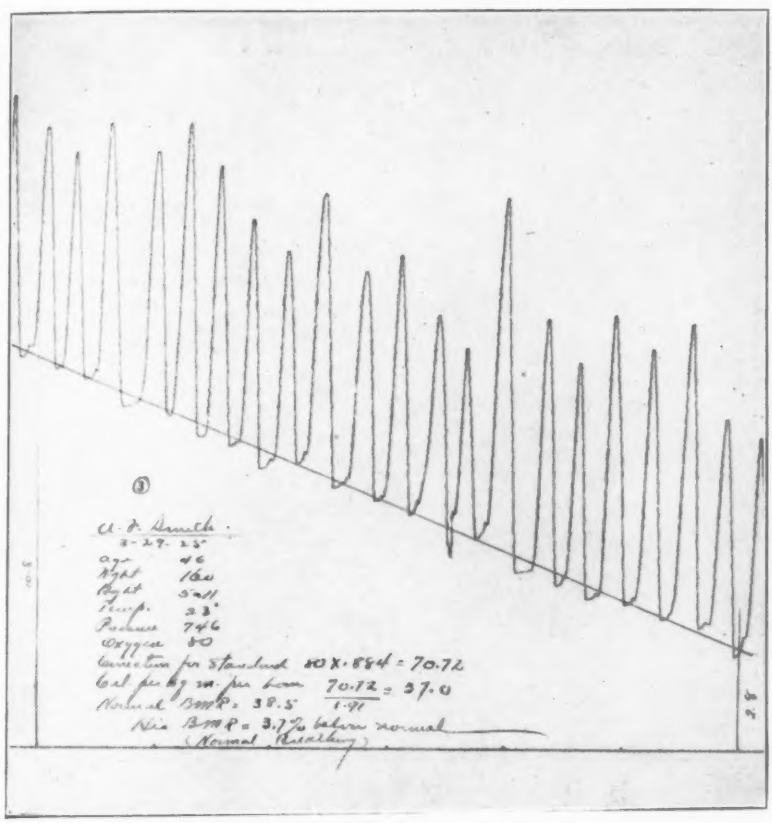

Fig. 5.—Patient A. F. S. Respiratory tracing during period of sinus rhythm and slow regular breathing—basal conditions. B. M. R. 3.7 per cent below normal. Respiratory rate 3.3 per minute. Heart rate 68 per minute.

creased work of the heart is responsible for the increased oxygen consumption.

In view of this simultaneous rise in both cardiac and respiratory rates during the rise in metabolism, we examined him again on another occasion with the view of evaluating the importance of the above two factors by estimating the basal metabolic rate during a period of artificially induced rapid breathing (tachypnea), but without change in the normal rhythm of his heart. Figs. 5 and 6 show

the result of this test—the metabolism being identical in both instances, 3.7 per cent below normal. In the control test the respiratory rate was 3.33 per minute, the heart rate 68 beats per minute; in the artificially produced tachypnea the respiratory rate was 28 per minute and the cardiac rate 78. From this experiment we would conclude therefore that the increase in metabolism occurring during the period of paroxysmal tachycardia was associated rather with the increased

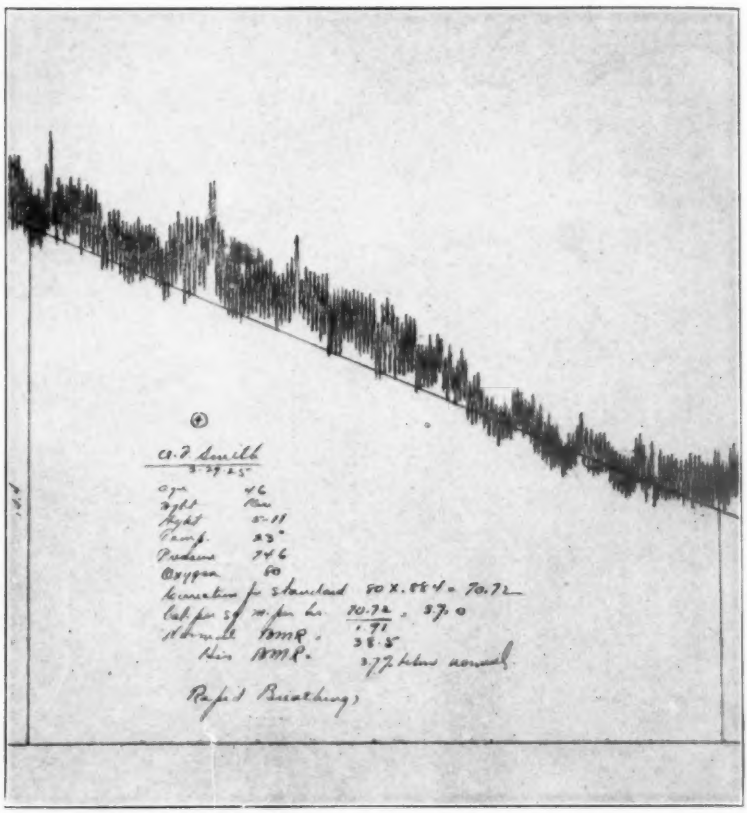

Fig. 6.—Subject A. F. S. During artificial induced rapid breathing (tachypnea). Note rapid but shallow excursions as compared with control (Fig. 5). B. M. R. 3.7 per cent below normal. Respiratory rate 28 per minute. Heart rate 78 per minute.

cardiac activity than with the increase in respiratory rate. However the period of artificially induced tachypnea of this experiment was accompanied by rapid, extremely *shallow* breathing, as may be seen in the graph (Fig. 6).

Summarizing then the results of this experiment we find a rise of 11.1 per cent in the basal metabolic rate, an increase of 2.5 times in the pulse rate and of 1.7 times in the respiratory rate, during the period of rapid heart action in a case of paroxysmal auricular tachy-

cardia. Increasing artificially the respiratory rate (tachypnea) to 8.5 times the normal, but with shallow breathing, causes no change in basal metabolism. One would conclude therefore that the increase in metabolic rate is dependent more on the increased rate of the heart than on the increased rate of respiration.

Attempting to substantiate this conclusion and to gain further data

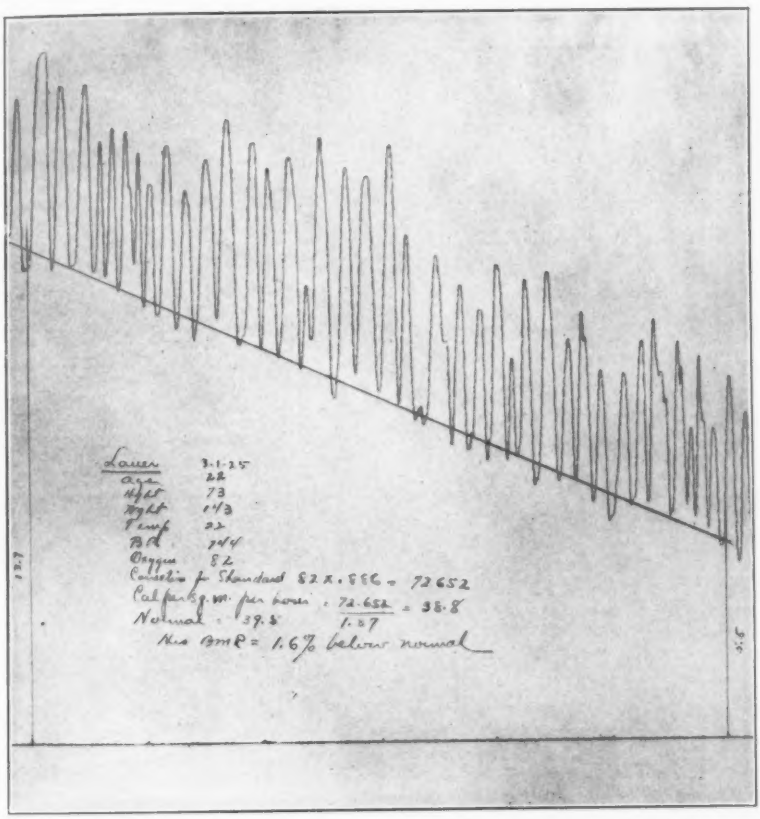

Fig. 7.—Subject L. Normal respiratory curve (control). B. M. R. 1.6 per cent below normal. Respiratory rate 6.6 per minute. Heart rate 70 per minute.

relative to the effect of tachypnea alone on the basal metabolic rate, we made certain further experiments on other subjects. In the case of Subject L, a young medical student of twenty-two years, his basal metabolic rate with normal breathing of 6.6 times per minute was 1.6 per cent below normal. Artificial tachypnea to a rate of 20 respirations per minute, with about equal depth of respiratory excursion, showed a rate of 15.9 per cent above normal—a total increase of 17.5 per cent (Figs. 7 and 8). This result then, with tachypnea of equal depth as the control, shows a definite increase in the basal

metabolic rate, with only slight change in cardiac rate from 70 to 76 beats per minute.

DISCUSSION

Summarizing the results of these observations it appears that two factors at least are operative in the production of increased basal metabolic rate under these conditions, i.e., tachycardia and tachypnea. They offer no definite information as to the relative importance of

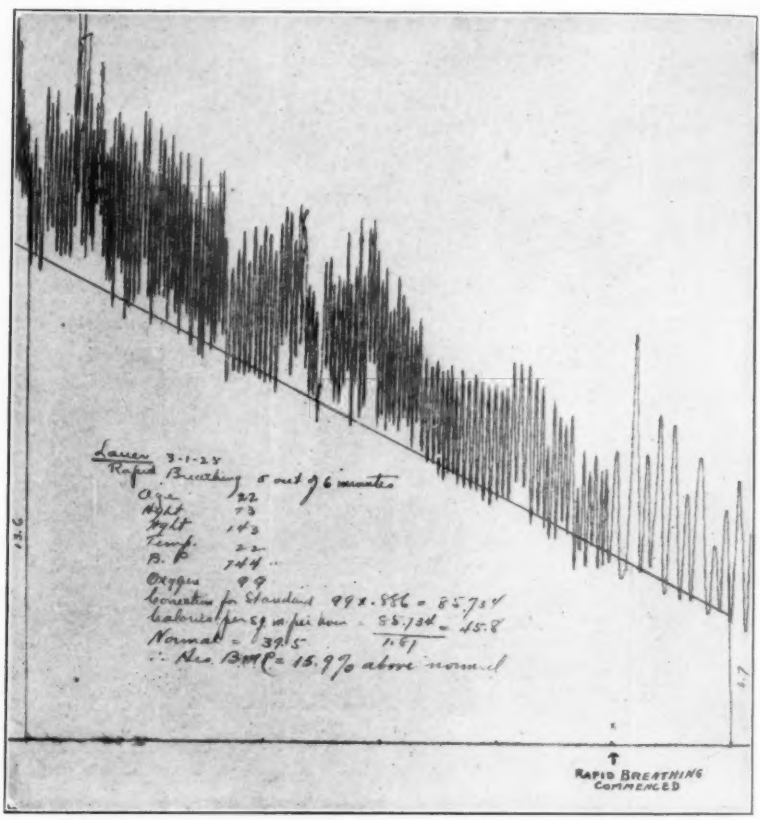

Fig. 8.—Subject L. Respiratory curve during artificially induced rapid breathing. (Artificial tachypnea.) B. M. R. 15.9 per cent above normal. Respiratory rate 20.1 per minute. Heart rate 76 per minute.

these two factors although "Lowey estimates that heart action accounts for 3.6 per cent of the metabolism of men and the respiratory movements for about 10 per cent."[5] Attempts to correlate these findings with the basal metabolic rate and respiratory rate of patients with organic heart disease with decompensation (dyspnea) indicate that the same two factors are operative here; although one gains the impression that there may be present also some additional and more fundamental factors, such as lactic acid accumulation from incomplete

oxidation (Lusk)[7] carbon dioxide acidosis (Peters and Barr),[8] or changes in the thyroid circulation from long standing congestion of the superior circulation (transient hyperthyroidism during decompensation).

CONCLUSIONS

1. Seventy-five per cent of the cases of organic heart disease with decompensation show an increased basal metabolic rate of an average of 39 per cent above normal.

2. The increase in basal metabolic rate is not related directly to the type of heart involvement, arrhythmia, cyanosis or edema, but seems to vary only with the degree of decompensation and the cardiac and respiratory rate.

3. The high basal metabolic rate decreases gradually with the return of compensation, but remains high or goes higher as decompensation continues or becomes more pronounced.

4. In a case of paroxysmal tachycardia the basal metabolic rate increased 11.1 per cent during the paroxysm.

5. In a normal subject, artificially induced tachypnea resulted in a 17.5 per cent basal metabolic rate increase.

6. It is probable that the increased work of the heart and the increased activity of the muscles of respiration are responsible for the increase in basal metabolic rate in organic heart disease with decompensation, although the possibility of other factors may be considered, notably a thyroid factor, from transient hyperthyroidism during decompensation, or changes in the thyroid circulation from long standing congestion of the superior circulation.

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Albion Walter Hewlett

The recent untimely death of Doctor Hewlett, at the age of fifty years, has brought to a sadly early close a career that was in many ways remarkable. Few men in the profession of medicine have shaped their lives with greater singleness of purpose and loftiness of ideals. As a fruitful investigator, a sound and stimulating teacher and a clear and logical writer, he contributed generously to the advancement of scientific medicine in this country. His treatise, *Pathological Physiology of Internal Diseases,* has become a classic in its field. As Professor of Medicine, first at the University of Michigan and later at Stanford University, he left the imprint of his modest, gentle bearing and his earnest, eager, scientific spirit upon every one who came within his range of influence. American medicine, no less than his wide circle of personal friends, has suffered grievous loss in the death of Walter Hewlett. This loss is shared by the AMERICAN HEART JOURNAL and its editorial staff, of which he was an honored member.

Department of Reviews and Abstracts

Selected Abstracts

Cohn, Alfred E. and Stewart, Harold J.: Evidence that Digitalis Influences Contraction of the Heart in Man. Jour. Clin. Investigation, 1924, i, 97.

The effect of digitalis in therapeutic doses was studied in patients by the method of a moving x-ray film. The patient faces a lead screen in which a transverse slit 1 cm. wide is cut, and placed opposite that portion of the border of the left ventricle which exhibits the greatest excursion; the x-ray film is raised past the slit on the other side of the screen while being exposed to an x-ray tube 36 inches from the screen. A record was obtained showing a continuous curve, the trough being systole and the crest diastole. The distance between the two positions was used as a measure of the degree of ventricular contraction or shortening.

Four patients were studied, who were free from edema and with reasonably thin chests. Two of these exhibited a normal rhythm and the other two that of auricular fibrillation.

There were seen no significant or consistent changes in either the systolic or diastolic blood pressure. In all cases a significant increase in the height of the left ventricular excursion was seen when the patients were under the influence of digitalis. As the effect of the drug wore off the height of the excursion decreased. As a rule no decrease in the size of the heart took place.

Hamilton, Burton E.: I. The Heart in Toxic Thyroid States. II. Heart Failure (Congestive) Associated with Thyroid Toxicity. Surg. Clin. N. Amer., 1924, iv, 1411 and 1425.

In these two clinical discussions of the heart in toxic thyroid states one will find a very clear presentation of this interesting and important subject. However one may differ from the views here expressed, the reader is easily impressed by the important factors recorded which may help in the understanding of the relationship of the heart and its function to toxic goiter.

It is most instructive to note the clear reasoning employed in arriving at the various conclusions, without the aid of elaborate laboratory procedures. This is of great importance to the average clinician. The lesson to be learned in this report should be of great value to practitioners who have not the opportunity for as wide an experience as the author.

Burwell, C. Sidney, and Robinson, G. Canby: A Method for the Determination of the Amount of Oxygen and Carbon Dioxide in the Mixed Venous Blood of Man.

Jour. Clin. Investigation, 1924, i, 47.

The technical contributions which are made in this report consist in the employment of alveolar air samples obtained by the Haldane-Priestly method after adjustment of the lung air, in order to determine the proper gas mixture to be used for diluting the lung air; the double rebreathing method for determining the correctness

of the oxygen tensions in the rebreathing bag; the method of obtaining a gas mixture in which all gases are in equilibrium with those of the venous blood; and the direct use of this gas mixture for obtaining so-called mixed venous blood by equilibration in a tonometer.

This method for obtaining the gaseous content of the mixed venous blood of healthy resting subjects fulfills all requirements of known physiological facts. When the results of the method are combined with those of analysis of the arterial blood and of the determination of the gas exchange in the lungs data are at hand for calculating the output of the heart, per minute and per beat.

Levine, S. A.: Cases of Coronary Occlusion, with Recovery. Med. Clin. N. Amer., 1924, viii, 1719.

The author discusses the clinical diagnosis of angina pectoris and coronary occlusion and the differentiation between the two. The description is clear, complete and useful for the student of medicine. While the individual case may present features not so easily classified, and with the diagnosis not so easily made as one is led to believe in the report, still it will serve as a guide for working out the diagnosis. Five cases are reported, illustrating the important clinical features that occur. Attacks of coronary closure are not uncommon and can easily be recognized by the physician with no other means than those he has constantly at the bedside. They must be clearly differentiated from the ordinary attacks of angina pectoris, for the prognosis and treatment of the two conditions are quite different. It is important to bear in mind that recovery frequently occurs and that patients are even restored to their active duties.

Burwell, C. Sidney, and Robinson, G. Canby: The Gaseous Content of the Blood and the Output of the Heart in Normal Resting Adults. Jour. Clin. Investigation, 1924, i, 87.

Data obtained by determination of the oxygen and carbon dioxide content of the mixed venous blood, by measuring the gas exchange in the lungs, and by counting the pulse allow the estimation of the output of the heart per minute and per beat. The authors consider that the circulation minute volume calculated from the oxygen figures is more reliable than that calculated from the carbon dioxide figures.

Their studies indicate that the usual minute output of the normal resting adult is 3,500 to 4,500 c.c. and the usual output per beat is 60 to 70 c.c.; but exceptions occur and individuals under otherwise constant conditions may show variations from 6,700 to 4,500 c.c. Quantitative studies of such a matter as the output of the heart, therefore, are better studied as individual results than as averages.

From the tables reported, it is apparent that neither the minute output nor the output per beat has any exact or noteworthy relation to body weight, to body surface area, or to the volume of oxygen absorbed. The authors insist on the relationship which must exist between the minute output and basal metabolic rate and exercise.

Dublin, Louis I., Fisk, Eugene Lyman, and Kopf, Edwin W.: Physical Defects as Revealed by Periodic Health Examinations. Amer. Jour. Med. Sci., 1925, 170, 576.

As part of the work of the Life Extension Institute, the examinations on 16,662 white males, supposedly able to work, are reported. The proportion of advanced and serious defects is found to be highest at the older age groups, while minor and moderate defects are common among young men.

The heart examinations showed no material difference between overweights and normal weights with respect to valve damage but there was a higher proportion of enlarged hearts, (3.4 per cent) and pulse above 90 (10.9 per cent) among overweights than in persons of normal weight (2.5 per cent and 7.1 per cent, respectively). Persons definitely overweight show smaller percentage of arterial thickening than do normals, and yet the proportion of persons with blood pressures 20 to 40 mm. above normal for age was 12.8 per cent among those who were overweight as compared with 5.2 per cent among normals. This close relationship between high blood pressure and overweight is exceedingly significant, particularly at the middle-age period.

Examination revealed conditions abnormal in some degree with respect to heart and pulse in 17.2 per cent of the cases. Functional murmur or irregularity occurred in 6 per cent, organic murmur in 1 per cent, heart enlargement in 2.7 per cent, and rapid pulse (above 90) in 8.3 per cent, with slow pulse (below 58) in 1.4 per cent. These cases of heart murmur and enlargement are notably more frequent among the older age group. Slow pulse, likewise, is more common in the older age groups and among low blood pressure groups.

The difference in blood pressure classification between those who are listed as "temperate" and "excessive" users of tobacco and as nonusers is only slight. Among 5,520 cases of excessive tobacco users there were no excess ratio of high blood pressure cases, although other important impairments were found, such as increased ratio of arterial thickening, mouth infection and rapid pulse.

Most of the defects and impairments discovered in the younger ages of adult life are subject to effective control, especially in the field of weight control. These figures show conclusively that marked overweight is associated with serious impairment of cardiovascular function, and this suggests that recognition and control of excessive body weight may lead to a sharp reduction in the actual number of individuals with embarrassed hearts and blood vessels.

Thayer, Wm. S.: Reflections on the Interpretation of Systolic Cardiac Murmurs. Am. Jour. Med. Sci., 1925, clxix, 313.

Before one jumps to a consideration of cardiac murmurs in the abstract, it would be better to try to decide what may be the cause of the sound in the concrete case on the basis of simple anatomical, physical and physiological phenomena. With this view in mind, the author explains the simple physical conditions on which a cardiac murmur may depend.

The aortic and pulmonary rings, more or less constant in circumference, connect the proximal ventricles, which may vary considerably in their strength and in the quantity of blood that they eject, with the distal vessels, which are of great elasticity and capable of wide dilatation. Nature has so admirably adjusted the ventricle ring and vessel that, in normal function, they act as if parts of one elastic tube of constant size. Murmurs then occur when the ventricle is dilated or hypertrophied, or wherever the aorta beyond the ring is relaxed or dilated, or whenever the ring itself is narrowed.

In the case of systolic pulmonary murmurs in the young, with elastic lungs and a large cardiac incisure, the conus may impinge close to, or directly on, the chest wall. This should reproduce exactly the conditions which exist experimentally when one presses a stethoscope against the conus.

The tricuspid and mitral rings also in normal function behave not as straits, but as parts of a common auriculoventricular canal. Only with actual stenosis of these orifices do audible or palpable vibrations arise while the blood is flowing in its normal course. Apical systolic murmurs are not generally of very great intensity

for the obvious reason that the points at which we are able to approach the heart with our stethoscopes are situated proximally to the point of origin of the murmur. They are commonly heard in axilla and back because, even though considerable lung tissue lies interposed between the heart and chest wall, the root of the left ventricle and the left auricle over which the murmur is of greatest intensity, lie posteriorly.

It is not likely that vegetations in themselves play any essential part in producing audible vibrations save, perhaps, the large thrombotic vegetations of a bacterial endocarditis. The early murmurs arising at the mitral orifice in acute rheumatic heart disease are not due to the endocarditis but to the relaxation of the mitral ring, due to myocardial change. It is only with the subsequent chronic thickenings and curlings of the valve curtains and shortening of the chordae tendineae that recognizable insufficiency and stenosis occur.

Briefly, the author arranges the facts to be considered when a given apical systolic murmur may depend on: (1) actual valvular disease; (2) dilatation of the mitral ring; (3) or functional.

Functional murmurs at the apex are explained at some length and the frequency of their occurrence is noted especially in the recumbent or left lateral position.

Wood, J. Edwin, Jr., and White, Paul D.: The Electrocardiogram in Uremia and Severe Chronic Nephritis with Nitrogen Retention. Amer. Jour. Med. Sci., 1925, clxix, 76.

Thirty-eight cases of uremia and severe chronic nephritis with increased blood nitrogen have been studied with reference to the electrocardiogram. There were 12 of the 38 cases with abnormal changes in the electrocardiogram resulting from the toxic effect of the products of uremia upon the heart muscle. These toxic effects act in some respects like digitalis.

Four of the 12 positive cases showed definite abnormalities of rhythm: (1) probable auricular standstill and idioventricular rhythm, later changing to auricular fibrillation; (2) sinoauricular block with ventricular escape, later varying from an ectopic auricular rhythm to ventricular escape or to atrioventricular nodal rhythm; (3)marked sinoauricular bradycardia, possibly sinoauricular block; (4) variable sinoauricular block and auriculoventricular block with rare dropped beats.

The heart rates were variable and the bradycardia commonly said to be present in uremia, was not observed in their series. In 4 cases there was abnormality of the QRS complex, indicating intraventricular block. The T-wave in Lead II was flat, diphasic or inverted in 7 of the 12 positive cases and unusually high in the other 5 cases. Pronounced left axis deviation was present in 6 cases. A review of these studies fails to show a common factor in either positive or negative group and the nature of the toxin causing the change in the heart muscle as well as any common factor is obscure. In general the positive cases seem to have a more advanced nephritis, as indicated by the hospital mortality, albuminuric retinitis, higher blood pressures, and apparently the greater incidence of edema.

Faber, Harold K. and Barnett, Anna F.: The Value of the Convalescent Home in the Management of Chorea Minor. Arch. Ped., 1925, xlii, 41.

Twelve cases of chorea treated at Stanford Convalescent Home show a few recoveries, dramatic in rapidity and apparent completeness, and the rest a slower but no less apparently complete recovery. The facilities of the convalescent home allow bed rest with nursing care until symptoms have entirely disappeared—a period of from four to ten weeks in severe cases—and a further period of ambulatory care with the patient under supervision, during which he can regain his full strength. With schooling provided during the latter period, the child

need not worry about the loss of time and probable loss of promotion. Prolonged supervision of convalescence, the maintenance of nutrition and the insistence on liberal periods of sleep and rest are of utmost importance. These requisites can nowhere be quite so well provided as in convalescent homes.

The authors wish to avoid any extravagant or unwarranted claims and cannot say that any one factor, such as heliotherapy, has been responsible for such results as have been observed.

Boas, Ernst P., and Perla, David: Mitral Stenosis after the Fifth Decade of Life. Amer. Jour. Med. Sci., 1925, clxx, 529.

During the last two and a half years, 183 patients of all ages were discharged or died at Montefiore Hospital with the diagnosis of mitral stenosis. Of these, 46 were over fifty years of age, the oldest being eighty-three. Seventeen gave a clear history of a typical rheumatic infection. Three others with no history of rheumatism should be included as at autopsy typical healed verrucae were found. Twelve patients remembered no rheumatic infections but showed signs of mitral stenosis.

Fourteen patients in a third group with one exception were over sixty years of age, in whom, too, there was no history of antecedent infections, but who, in addition to the physical signs of mitral stenosis, gave evidence of widespread arteriosclerosis of both peripheral and central vessels. These patients, as a rule, did not present the typical full blooded appearance of the ordinary mitral patient, but were more poorly nourished and of a more sallow complexion. In 3, various complications, such as cerebral hemorrhage, cerebrospinal arteriosclerosis and diabetes occurred. The authors venture to diagnose these cases as atherosclerotic mitral stenosis. The diagnostic features and the pathological changes in this type of mitral stenosis are discussed.

Of the 56 patients, 26 were accompanied by auricular fibrillation; 36 per cent of the atherosclerotic group in contrast to 70 per cent of the rheumatic group had this complication.

The 30 women had given birth to 119 children; only 6 had no children, while 2 had 10 and 1 had 12 offspring.

Stroud, Wm. D.: Care of Children Convalescing from Heart Disease. Arch. Ped., 1925, xlii, 190.

The author reports on the work which the Philadelphia Association for the Prevention and Relief of Heart Disease has been attempting for the care of children convalescing from infections which usually or occasionally damage the heart; some children with apparently damaged hearts, others with actually damaged hearts. This care consists of absolute rest, increased nutrition and the removal of foci of infection. Two weeks admission to a hospital ward are required for tonsillectomy and the eradication of definitely diseased teeth.

Four cases illustrative of the course of patients so treated are included.

The author feels that prolonged rest in bed, six to eight months, with a gradual increase in effort as the temperature, gain in nutrition and general improvement ensue, will not only greatly lessen the possibility of a reactivation of an endocarditis, but a recurrence of the original etiological factor as well.

Book Review

CLINICAL FEATURES OF HEART DISEASE.—By Leroy Crummer, M.D., Professor of Medicine, University of Nebraska. Pp. 353. Paul B. Hoeber, Inc., New York.

The author of this volume, like many others, found in the examination of candidates for the army a unique opportunity to increase his knowledge of heart conditions and to observe with accuracy many slight deviations from the normal. The subject matter of the book is based on "Circular 21" which was issued by the War Department for the instruction of medical officers in examining the heart and blood vessels of army recruits. This necessarily limits the scope of the book and, as might be expected, the clinical features of all types of heart diseases are by no means covered. But the book presents in admirably clear and concise form the clinical and diagnostic features of the more important types of cardiac disease. Careful history taking and the accurate observation of physical signs are stressed in a way that is refreshing in these days when so often x-ray plates, polygrams and electrocardiograms seem to have absorbed the interest of many practitioners to the exclusion of the less spectacular but more important methods of physical examination.

Doctor Crummer presents a number of unusual observations and offers suggestions for their interpretation which do not always conform to accepted opinions. His original views need not perhaps always be accepted as entirely sound, but they are evidently advanced only after painstaking observations and with a sincerity which must challenge the respectful consideration of the reader. The antagonism which some of his statements arouse is stimulating and in this is to be found one of the chief virtues of the book. Examples of his unusual points of view may be found in his discussion of the "first sound right" and the "first sound left" (chapter IV) and in his "block" method for the administration of digitalis to fibrillators (pp. 121, 259, 261).

More than once he takes a fling at dogmatism; even Osler and Mackenzie do not escape (p. 46). One who does this has all the greater need for caution as to his own statements; for example (p. 39), when one finds a tumor of the chest pulsating in heart rhythm, is a diagnosis of aneurysm "permanently established" until a localized empyema has been excluded? Or (p. 62) is a diastolic decrescendo murmur heard in second right interspace invariably diagnostic of aortic insufficiency?

Evidently the author is an expert not only in the study of physical signs but also in the psychology of the patient. Internal evidence indicates that he has taken care of many patients outside institutional walls, from whom he has learned much that the purely hospital and laboratory man has had little opportunity to acquire. His book has many helpful hints and suggestions as to the best methods of handling patients who have or think they have defective hearts.

T. S. H.